Minnesota M

Contents for Apr

SCIENTIFIC ARTICLES

ORIGINAL CONTRIBUTIONS

Value of Central and Peripheral Intra-arterial Pressures and Pulse Contours in Cardiovascular Diagnosis

J. Leo Wright, M.D., and *Earl H. Wood, M.D., Ph.D.,* Rochester, Minnesota 215

Noninflammatory Diseases of Smaller Arteries and Arterioles

Edgar A. Hines, Jr., M.D., Rochester, Minnesota 223

Raynaud's Disease

Ray W. Gifford, Jr., M.D., Rochester, Minnesota..... 226

Periarteritis Nodosa and Temporal Arteritis

Richard M. Shick, M.D., Rochester, Minnesota 231

Peripheral Vascular Diseases

Edgar V. Allen, M.D., Rochester, Minnesota 236

The Physiologic Action of Ganglionic and Adrenergic Blocking Agents on the Peripheral Circulation

Harold D. Green, M.D., Winston-Salem, North Carolina 2

Fundamentals of Anticoagulant Therapy

Nelson W. Barker, M.D., Rochester, Minnesota 2

Diagnosis and Treatment of Local Edema of Lower Extremities

John J. Fairbairn, II, M.D., Rochester, Minnesota.... 2

A New Concept in the Surgical Treatment of Aortic Insufficiency

J. J. Garamella, M.D., J. G. Andersen, M.D., R. Oropeza, M.D., N. K. Jensen, M.D., L. J. Hay, M.D., and *R. Naidu, M.D.,* Minneapolis, Minnesota 2

A New Antirheumatic Steroid

Paul J. Bilka, M.D., and *James C. Melby, M.D.,* Minneapolis, Minnesota 2

Owner and Publisher

MINNESOTA STATE MEDICAL ASSOCIATION
496 Lowry Medical Arts Building
St. Paul 2, Minnesota

Publishing and Finance Committee

E. M. Hammes, M.D.
Chairman, Saint Paul

F. M. Owens, Jr., M.D.
Saint Paul

T. A. Peppard, M.D.
Minneapolis

Henry Ulrich, M.D.
Minneapolis

Business Manager

R. R. Rosell
496 Lowry Medical Arts Building
St. Paul 2, Minnesota

Official Journal of

Duluth Surgical Society
Minneapolis Academy of Medicine
Minneapolis Obstetrical and Gynecological Society
Minneapolis Surgical Society

Minnesota Academy of Medicine
Minnesota Academy of Occupational Medicine and Surgery
Minnesota Obstetric and Gynecologic Society
Minnesota Society of Clinical Pathologists

Minnesota Society of Internal Medicine
Minnesota Society of Neurology and Psychiatry
Minnesota State Medical Association
Minnesota Surgical Society

Minnesota Trudeau Society
Northern Minnesota Medical Associati
Saint Paul Surgical Society
Southern Minnesota Medical Association

Minnesota M

Contents for Apr

SCIENTIFIC ARTICLES

ORIGINAL CONTRIBUTIONS

Value of Central and Peripheral Intra-arterial Pressures and Pulse Contours in Cardiovascular Diagnosis

J. Leo Wright, M.D., and *Earl H. Wood, M.D., Ph.D.,* Rochester, Minnesota 215

Noninflammatory Diseases of Smaller Arteries and Arterioles

Edgar A. Hines, Jr., M.D., Rochester, Minnesota 223

Raynaud's Disease

Ray W. Gifford, Jr., M.D., Rochester, Minnesota..... 226

Periarteritis Nodosa and Temporal Arteritis

Richard M. Shick, M.D., Rochester, Minnesota 231

Peripheral Vascular Diseases

Edgar V. Allen, M.D., Rochester, Minnesota 236

The Physiologic Action of Ganglionic and Adrenergic Blocking Agents on the Peripheral Circulation

Harold D. Green, M.D., Winston-Salem, North Carolina 2

Fundamentals of Anticoagulant Therapy

Nelson W. Barker, M.D., Rochester, Minnesota 2

Diagnosis and Treatment of Local Edema of Lower Extremities

John J. Fairbairn, II, M.D., Rochester, Minnesota.... 2

A New Concept in the Surgical Treatment of Aortic Insufficiency

J. J. Garamella, M.D., J. G. Andersen, M.D., R. Oropeza, M.D., N. K. Jensen, M.D., L. J. Hay, M.D., and *R. Naidu, M.D.,* Minneapolis, Minnesota 2

A New Antirheumatic Steroid

Paul J. Bilka, M.D., and *James C. Melby, M.D.,* Minneapolis, Minnesota 2

Owner and Publisher

MINNESOTA STATE MEDICAL ASSOCIATION
496 Lowry Medical Arts Building
St. Paul 2, Minnesota

Publishing and Finance Committee

E. M. Hammes, M.D.
Chairman, Saint Paul

F. M. Owens, Jr., M.D.
Saint Paul

T. A. Peppard, M.D.
Minneapolis

Henry Ulrich, M.D.
Minneapolis

Business Manager

R. R. Rosell
496 Lowry Medical Arts Building
St. Paul 2, Minnesota

Official Journal of

Duluth Surgical Society
Minneapolis Academy of Medicine
Minneapolis Obstetrical and Gynecological Society
Minneapolis Surgical Society

Minnesota Academy of Medicine
Minnesota Academy of Occupational Medicine and Surgery
Minnesota Obstetric and Gynecologic Society
Minnesota Society of Clinical Pathologists

Minnesota Society of Internal Medicine
Minnesota Society of Neurology and Psychiatry
Minnesota State Medical Association
Minnesota Surgical Society

Minnesota Trudeau Society
Northern Minnesota Medical Associati
Saint Paul Surgical Society
Southern Minnesota Medical Association

ta Medicine

for April, 1958

Volume 41
Number 4

MISCELLANEOUS ARTICLES

EDITORIALS

Infant Feeding 266
Trends in Medicine 267
Medical Librarians: What Do They Do? 268
Life Insurance in Estate Planning Today 269
Economic History 270
Education and State Government 271

PRESIDENT'S LETTER

A Most Rewarding Committee—Physician's Assistance 273

MEDICAL ECONOMICS

Minneapolis Tops U. S. on Medical Care Costs 274
Retail Druggists Testify on Behalf of Jenkins-Keogh Bill 274
Medicare Issues Rules on Drugs and ID Cards 274
Aged Lack Health Insurance 274
Disciplinary Act Upheld by Court 275
AMA Newspaper to Make Debut 275
AMA Grows 275
National Jaycees Health Program 275
U. S. Medical Post in Doubt 275
Arthritis Capsules Curbed 276
FDA Cracks Down on Quacks 276
United States—Russian Medical Scientist Exchange Plan 276
Barbiturate Refills Questioned 276
Fourteen Reasons Why the Forand Bill Should Not be Passed 276

MINNESOTA STATE MEDICAL ASSOCIATION

105th Annual Meeting—Preliminary Program 278

HISTORY OF MEDICINE IN MINNESOTA

A Medical History of Meeker County to 1900
Harold E. Wilmot, M.D., Litchfield, Minnesota 282

MINNESOTA BLUE CROSS-BLUE SHIELD 290

MEETINGS AND ANNOUNCEMENTS A-44

WOMAN'S AUXILIARY A-48

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS A-51

IN MEMORIAM A-52

CORRESPONDENCE A-53

GENERAL INTEREST A-54

BOOK REVIEWS A-61

GENERAL INFORMATION

Authors

Manuscripts should be addressed to Arthur H. Wells, M.D., Editor, 915 East First Street, Duluth 5, Minnesota. Telephone RA 7-6636 or JA 5-2319.

Readers and Reviewers

The right is reserved to reject material submitted for reading or advertising columns. The views expressed in this journal do not necessarily represent those of the Minnesota State Medical Association or any of its constituents.

Advertisers and Subscribers

Classified advertising—15 cents a word; minimum charge $3.00; key number, 25c additional. Remittance should accompany order. Display advertising rates on request.

Annual Subscription—$5.00. Single Copies—$0.50. Foreign and Canadian—$5.50.

Communications concerning advertising and subscriptions should be addressed to MINNESOTA MEDICINE, 2642 University Avenue, Saint Paul 14, Minnesota. Telephone Midway 6-2641.

Copyright and Post Office Entry

Contents of MINNESOTA MEDICINE © 1958 by Minnesota State Medical Association.

Entered at the Post Office in Saint Paul as second class matter. Accepted for mailing at the special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized July 13, 1918.

Board of Editors

ARTHUR H. WELLS, M.D.
Editor-in-Chief, Duluth

STUART W. ARHELGER, M.D.
Minneapolis

JOHN F. BRIGGS, M.D.
Saint Paul

S. FRANCIS CEPLECHA, M.D.
Redwood Falls

TAGUE C. CHISHOLM, M.D.
Minneapolis

N. L. GAULT, JR., M.D.
Minneapolis

R. DREW MILLER, M.D.
Rochester

HENRY G. MOEHRING, M.D.
Duluth

GLENN J. MOURITSEN, M.D.
Fergus Falls

OLIVE V. SEIBERT, B.A.
Saint Paul

GEORGE STILWELL, M.D.
Rochester

WHEN YOU TREAT INFECTIONS IN PATIENTS SUCH AS THESE

- debilitated
- elderly
- diabetics
- infants, especially prematures
- those on corticoids
- those who developed moniliasis on previous broad-spectrum therapy
- those on prolonged and/or high antibiotic dosage
- women—especially if pregnant or diabetic

the best broad-spectrum antibiotic to use is

MYSTECLIN-V

Squibb Tetracycline Phosphate Complex (Sumycin) and Nystatin (Mycostatin) — Sumycin plus Mycostatin

for practical purposes, Mysteclin-V is sodium-free

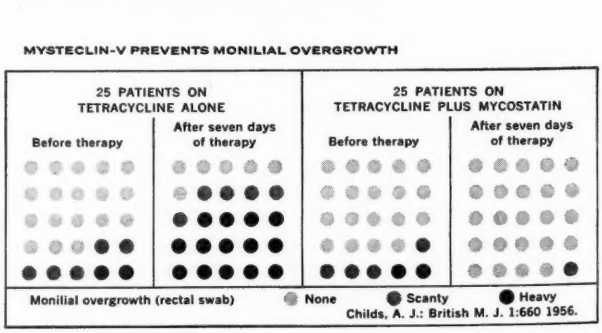
for "built-in" safety, Mysteclin-V combines:

1. Tetracycline phosphate complex (Sumycin) for superior initial tetracycline blood levels, assuring fast transport of adequate tetracycline to the infection site.

2. Mycostatin—the first safe antifungal antibiotic—for its specific antimonilial activity. Mycostatin protects many patients (see above) who are particularly prone to monilial complications when on broad-spectrum therapy.

Capsules (250 mg./250,000 u.), bottles of 16 and 100. *Half-Strength Capsules* (125 mg./125,000 u.), bottles of 16 and 100. *Suspension* (125 mg./125,000 u.), 2 oz. bottles. *Pediatric Drops* (100 mg./100,000 u.), 10 cc. dropper bottles.

MYSTECLIN-V PREVENTS MONILIAL OVERGROWTH



Childs, A. J.: British M. J. 1:660 1956.

SQUIBB

Squibb Quality—the Priceless Ingredient

"MYSTECLIN," "MYCOSTATIN," AND "SUMYCIN" ARE SQUIBB TRADEMARKS

Original Contributions

Value of Central and Peripheral Intra-arterial Pressures and Pulse Contours in Cardiovascular Diagnosis

J. LEO WRIGHT, M.D.
EARL H. WOOD, M.D., Ph.D.
Rochester, Minnesota

INTRA-ARTERIAL pressure was first measured in man in 1856 by Jean Faivre,[1] a senior intern at the Hôtel Dieu in Lyon, France. The pressure in the arteries of three patients undergoing amputation of limbs was measured by connecting the proximal end of the cut artery to a U-shaped mercury manometer similar to the type previously used by Poiseiulle. The subsequent history of the measurement of intra-arterial pressure and pulse contours for diagnosis is really a history of the introduction and improvement of instruments and recording methods designed for the faithful reproduction of pressure and pulse contours.[2-7]

Until the 1930's, however, the clinical use of intra-arterial pressure measurement in man was infrequent and was conducted with caution during blood transfusions, during amputations[8] and in terminally ill patients.[9] In 1931, Wolf and von Bonsdorff[10] reported study of pressures recorded by means of percutaneous needle puncture of the brachial artery in fifteen persons; in 1932, Dameshek and Loman[11] reported similar measurements in approximately 150 patients in a state hospital. The primary purpose of these studies was a comparison of intra-arterial pressures with the readings obtained by indirect cuff methods.

Since 1946, more than 2,000 percutaneous punctures of the radial artery[12] have been done at the Mayo Clinic in the Cardiovascular Laboratory, Section of Physiology. This work includes normal persons, infants and adults undergoing diagnostic cardiac catheterization, as well as patients undergoing special studies of intra-arterial pressure. The sequelae of arterial puncture have been minor. Careful periarterial infiltration with procaine has controlled pain adequately. Hematoma, a potential complication, has not been encountered when pressure over the artery is maintained after withdrawal of the needle. Minimal tenderness over the site of puncture has been experienced by some patients for twenty-four to forty-eight hours.

During cardiac catheterization, indwelling intra-arterial needles are routinely used for monitoring pressure and for withdrawing samples of blood for oxygen determination at rest and during exercise.[13] Intra-arterial needles are also used for continuous recording of arterial indicator-dilution curves[14,15] and may be left in place for hours without discomfort or hazard to the patient. Obvious additional clinical applications are determinations of intra-arterial blood pressure in extremely obese patients or patients who have severe arteriosclerosis of peripheral arteries, both of which groups tend to give unreliable readings of blood pressure when it is determined by the indirect method. Other particularly valuable uses of this technique are (1) continuous monitoring of blood pressure during operations on the heart,[16,17] (2) measurement of the pressure distal to the aortic valve during catheterization of the left side of the heart[18] and (3) localization of abnormal obstructions of the circulation, which will be discussed later in the text.

Methods

Pressure pulses were recorded utilizing photokymographic recording methods with strain-gauge manometers.[7] In peripheral arteries, such as the radial, brachial, femoral, dorsalis pedis or posterior tibial, pressures were obtained by direct arterial puncture using special, internally polished,

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 23, 1957.

Dr. Wright, former Assistant to the Staff, is now Director, Cardio-Pulmonary Laboratory, Baptist Memorial Hospital, Memphis, Tennessee. Dr. Wood is from the Section of Physiology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

20-gauge needles. Arterial catheters were used for the simultaneous recording of central pressures in the aorta and branches of the aorta. These catheters, which have internal and external vessels of the arms; it also undergoes changes that are not exactly similar as it moves peripherally in the lower extremities. At the same time, important changes in pressure occur. It is evident

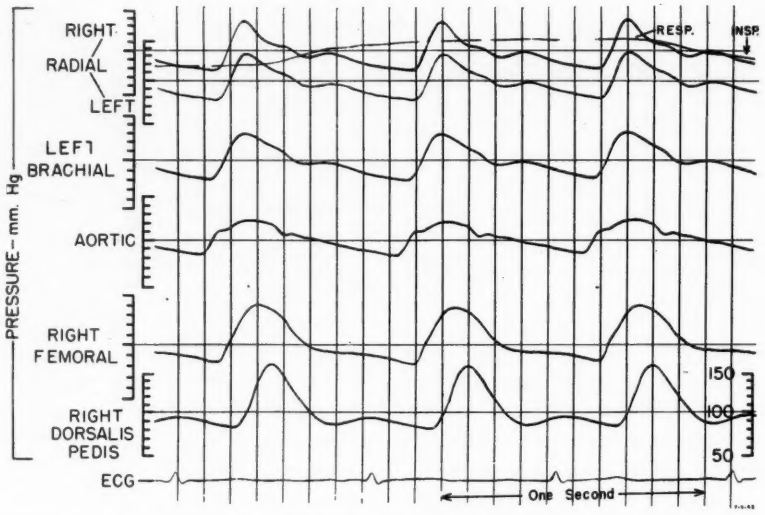


Fig. 1. Pulse contours in a healthy thirty-one-year-old man. Pressure pulses were recorded simultaneously in the right and left radial, left brachial, aortic arch, right femoral and right dorsalis pedis arteries. A reference line (100 mm. of mercury) is drawn through each series of pulses. The contour of the aortic pulse is significantly changed as the pulse wave moves peripherally into the arm. Somewhat different changes are observed as the pressure pulse generated by the same heartbeat moves peripherally into the leg. The associated increase in systolic pressure is greater in the more distally located dorsalis pedis artery than in the radial artery.

diameters of 0.5 and 0.8 mm., respectively, can be advanced readily into the arterial system through thin-walled 19-gauge needles after puncture of the radial or femoral artery. Larger catheters similarly introduced and routinely used for physiologic studies requiring the injection of dyes are equally suitable for recording arterial pressures.

For practical purposes, optimally damped recording systems having a uniform response to frequencies up to 10 cycles per second (cps) are adequate for recording arterial pressure, although manometer recording systems having response characteristics of $\pm$ 10 per cent of the static sensitivity up to 40 cps are routinely used in the laboratory.[19-21]

Pulse Contours in Healthy Persons

The differences in pressures and pulse contours generated by the same heart beat when recorded simultaneously at multiple sites in a normal adult are shown in Figure 1. It will be noted that the contour of the aortic pulse undergoes pronounced transformation as it moves peripherally in the that the systolic pressure increases as the pulse wave moves peripherally. However, the diastolic and mean pressures decrease slightly.

Figure 2 is a simplification of the previous figure in that only pressure pulses recorded between the aortic arch and the radial artery are shown. These contours were obtained in a healthy person by means of an arterial catheter introduced via a needle in the radial artery. Aortic pressure recorded by a second catheter introduced through a needle in the femoral artery and the radial pressure in the opposite arm were used as controls during the gradual withdrawal of the first catheter. The subclavian contour is characterized by an initial wave, a plateau type of systolic maximum, followed by a dicrotic halt, after which is seen a small postdicrotic wave. As the pulse wave moves out into the arm, the initial wave becomes steeper and larger in magnitude, the maximal pressure becomes peaked and the dicrotic halt tends to move down and out. At the radial artery, the wave that occurs between the systolic maxi-

mum and the dicrotic halt appears to be a remnant of the plateaulike maximum of the subclavian contour. The small aortic postdicrotic wave disappears shortly after the pulse wave enters the subclavian-radial system.

In Figure 3, simultaneously recorded radial and aortic pressure pulses in a healthy person are superimposed to illustrate the changes in pressure and contour between the two sites. Since the two strain gauges used to record the aortic and radial pulses had the same sensitivities, the calibration applies to both. Note the significantly greater aortic diastolic pressure. In this person, the radial systolic pressure was approximately 12 per cent greater than the aortic systolic pressure. In fifteen healthy persons, the radial systolic pressure averaged 12 per cent greater than did the simultaneously recorded aortic systolic pressure, the range being from 2 to 21 per cent. The diastolic and mean pressures decreased an average of 4 per cent, the ranges being −10 to 0 and −9 to −1 per cent, respectively. Similar results from a different series of persons have been obtained previously in this laboratory.[22]

Pulse Contours in Cardiovascular Diseases

Valvular Aortic Stenosis.—In Figure 4, the aortic and radial contours in a patient who had severe valvular aortic stenosis are superimposed. The aortic diastolic pressure is slightly greater than the radial diastolic pressure, as in normal persons. Unlike the normal state, however, the two contours are remarkably similar, an abnormal anacrotic pause is seen on the radial contour, the increase to the systolic maximum is greatly prolonged in both pressure pulses and, in pronounced contrast to the normal state, the radial systolic pressure is less than the aortic systolic pressure. Finally, a postdicrotic wave is not identifiable on the aortic contour. Our observations indicate that the central postdicrotic wave is present on pressure pulses recorded near a normally functioning aortic valve but that it usually is absent in patients who have significant aortic valvular disease.

Subvalvular Aortic Stenosis.—In Figure 5, pressure pulses obtained during catheterization of the left side of the heart in a patient with valvular aortic stenosis are compared with similar contours from a patient with subvalvular aortic stenosis. Evidence of severe obstruction to left ventricular outflow is present in both patients. The radial pulses are equally abnormal in contour. The aortic contour in the patient with subvalvular stenosis resembles a normal contour to a surprising degree. The postdicrotic wave on the

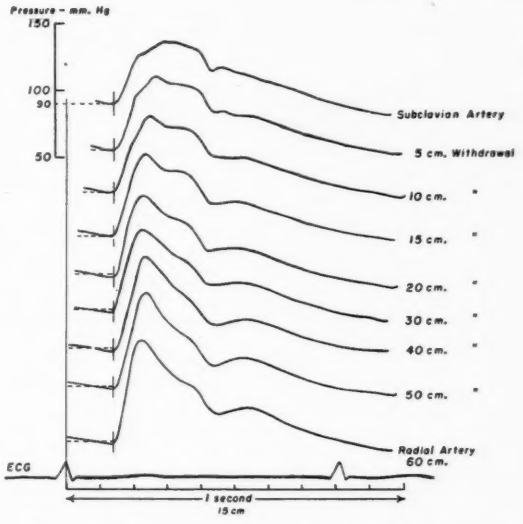


Fig. 2. Pulse contours in a healthy thirty-year-old man, showing transformation of the pressure pulse in the subclavian-radial system. Pressure pulses were recorded consecutively during withdrawal of the tip of an arterial catheter from the subclavian artery near the aorta to the radial artery in the left arm. The onset of each pressure pulse is aligned for purposes of comparison. As the pulse wave moves peripherally, the initial wave steepens and increases in magnitude, the dome-shaped systolic maximum becomes peaked, the dicrotic halt moves down and to the right and becomes slurred. The low-amplitude, central postdicrotic wave is not seen after the catheter has been withdrawn 10 cm. or more. The prominence of the radial dicrotic wave is due, in part, to the change in position of the dicrotic halt (see Figure 3). The horizontal dashed line intersecting the onset of each pulse contour is the calibration reference point (90 mm. of mercury). The interval of time from the peak of the R wave of the electrocardiogram to the onset of the systolic upswing of each pulse wave is indicated by the duration of each tracing to the left side of the short vertical lines, which mark the onset of systole for each pulse. These pulses are photostatic copies of pulses selected from the original photographic records on the basis that the contours of the aortic pressure pulses recorded simultaneously from a second arterial catheter, the phase of the respiratory cycle and the electrocardiogram were all closely similar.

aortic contour, which suggests a normally functioning aortic valve in the patient with subvalvular aortic stenosis, is absent in the patient with valvular stenosis. These diagnoses were confirmed surgically, and both lesions were successfully corrected.

Aortic Insufficiency.—In Figure 6, simultaneously recorded aortic and radial pressure pulses

in a patient who had severe aortic insufficiency are superimposed. The aortic diastolic pressure, as in the normal state, is slightly greater than the radial diastolic pressure. The diagnostic features of aortic insufficiency are (1) a low diastolic pressure, in this instance less than 50 mm. of mercury, (2) a wide pulse pressure and (3) a rapid rise to a peaked radial systolic pressure. In addi-

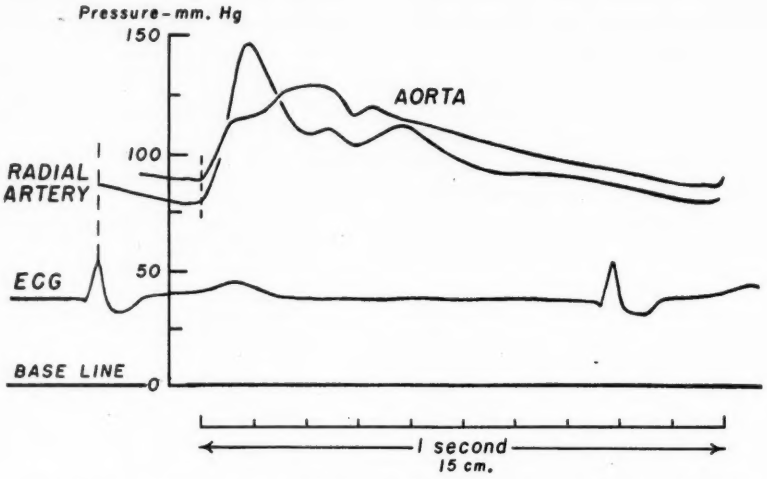


Fig. 3. Pulse contours in a healthy thirty-year-old man. Pressure pulses were recorded simultaneously in the aorta and radial artery, utilizing strain gauges having equal sensitivities. For purposes of comparison, photostatic copies of individual pulses were superimposed, with the onset of the pressure pulses aligned. The time interval between the peak of the R wave of the electrocardiogram and the beginning of the recording of the aortic pulse approximates the transmission time from the aorta to the radial artery. The increase in systolic pressure at the radial artery is the only portion of the pressure wave that exceeds the simultaneously recorded aortic pressure pulse. The remaining elements of the radial pressure wave are less than the aortic pressures. The pressure pulses shown in Figures 2 and 3 were recorded from different persons.

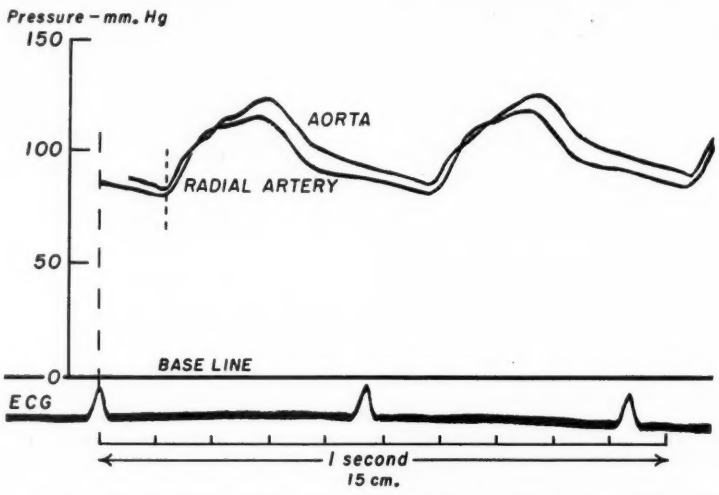


Fig. 4. Pulse contours in a twelve-year-old boy who had severe valvular aortic stenosis. The simultaneously recorded aortic and radial pressure pulses have been photostated and superimposed as in Figure 3. Note the similarity of the two contours, the decreased systolic pressure, the anacrotism of the radial pulse (lower tracing) and the absence of the central postdicrotic wave of the aortic contour (compare with Figures 2 and 3).

tion, the absence of both a well-defined dicrotic halt and a postdicrotic wave on the aortic contour strongly supports the diagnosis of aortic insufficiency.

Figure 7 compares the preoperative radial and femoral pressures with similar pressures recorded in the same patient two weeks and again five years after operation for coarctation. The classic

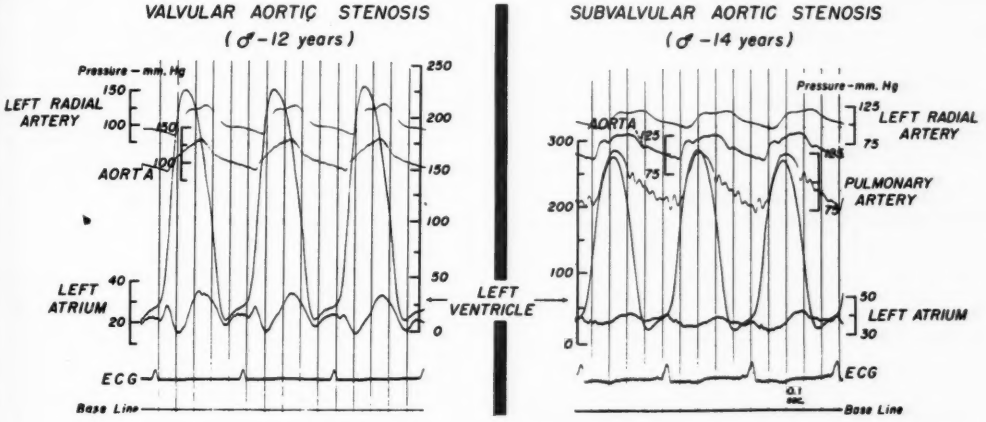


Fig. 5. Pulse contours in a twelve-year-old boy with valvular aortic stenosis compared with similar contours in a fourteen-year-old boy with subvalvular aortic stenosis. Simultaneously measured radial, aortic, left ventricular and left atrial pressures were recorded during percutaneous catheterization of the left side of the heart. The left ventricular systolic pressure is 125 to 150 mm. of mercury greater than the aortic systolic pressure in both patients, indicating severe obstruction to left ventricular outflow. Pronounced anacrotism of both radial pulse contours is evident. However, the aortic pressure pulse in the patient with subvalvular aortic stenosis resembles a normal aortic contour. In addition, a small central postdicrotic wave is easily identified; while not a proved diagnostic sign, this finding suggests the presence of a normally functioning aortic valve. Note the absence of left atrial-left ventricular pressure differences across the mitral valve during diastole, which excludes the presence of mitral stenosis.

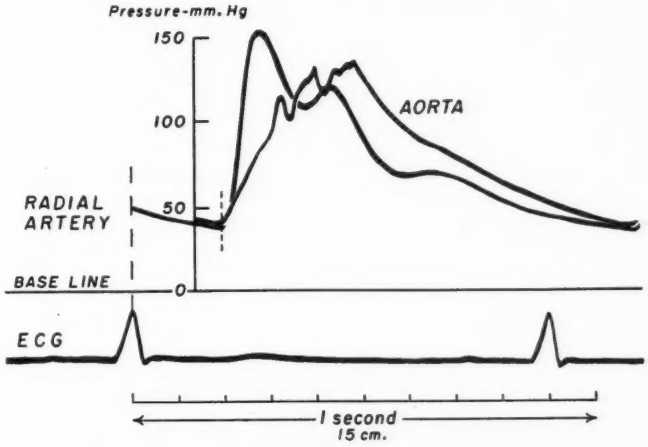


Fig. 6. Pulse contours in a twenty-four-year-old man who had aortic insufficiency. Aortic and radial pressure pulses were recorded simultaneously, utilizing strain gauges having equal sensitivities. The pulses have been photostated and superimposed for comparison as in Figure 3. The contours are characterized by a low diastolic pressure and wide pulse pressure. The radial upstroke is abrupt. The dicrotic halt of the aortic contour is slurred, and a well-defined postdicrotic wave cannot be identified.

Coarctation of the Aorta.—Obstruction in the aorta caused by coarctation produces characteristic changes in pressures and pulse contours. findings in coarctation of the aorta are (1) hypertension in the upper extremities, (2) a characteristic "saw-tooth" contour of small amplitude in

the tracing from the femoral artery, (3) a delay in arrival of the onset of the pulse at the femoral artery and (4) a great decrease in the ratios of femoral/radial systolic and pulse pressure to far

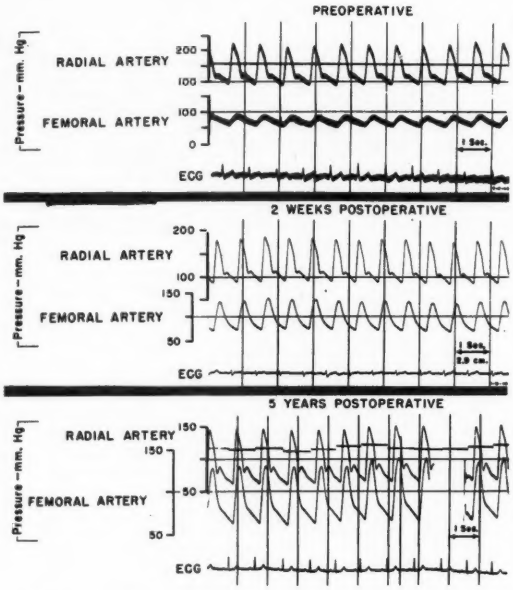


Fig. 7. Pulse contours in coarctation of the aorta. Radial and femoral pressure pulses were recorded simultaneously above and below the site of coarctation at a paper speed approximately one sixth as fast as in the other figures. *Upper panel (preoperative):* hypertension above the coarctation is associated with the characteristic "saw-tooth" femoral contour. The pulse pressure of the latter is small, and the diastolic pressure is less than the diastolic pressure above the coarctation. *Middle panel (two weeks after operation):* after resection of the coarctation and end-to-end anastomosis of the aorta, the hypertension above the site of resection is slightly less. The femoral pulse has changed from a "saw-tooth" appearance toward a more normal contour. However, both the systolic and diastolic pressures are significantly less than the radial pressures. *Lower panel (five years after operation):* the radial and femoral contours are within the range of normal. The systolic and diastolic pressures above and below the resected zone are now essentially the same.

below the range of normal. The significant decrease in radial systolic and diastolic pressures two weeks after operation is followed by a further striking decrease in radial pressure during the next five years. Concomitantly, a change toward normal occurs in the femoral contour and pressures, so that essentially no difference exists between the pressures in radial and femoral arteries at the five-year study. Another record of the changes caused by surgical correction of coarctation is seen in Figure 8. In a group of ten patients studied preoperatively and again four to seven years after resection of the site of coarctation and end-to-end anastomosis of the aorta, slight but continued improvement in the pressures measured above and below the site of resection was demonstrated.[23]

Systemic Hypertension.—In Figure 9, the radial and aortic pressures are compared in a patient who had hypertension caused by unilateral renal disease. The intra-arterial pressures recorded preoperatively ranged from 190/130 to 210/140. Following nephrectomy, this patient became normotensive.

No characteristic diagnostic changes have been recognized in central or radial pulse contours in the limited number of patients with systemic hypertension studied in the laboratory. Several nonspecific abnormalities in pulse contour in Figure 9 are noted. The radial contour is abnormal and, when viewed alone, might suggest valvular aortic stenosis. Viewed together with the normal aortic contour, especially when associated with an absence of amplification of the systolic pressure at the radial artery, it might suggest subvalvular aortic stenosis. Against this are the severe hypertension, wide pulse pressure, rapid build-up time and the large amplitude of the initial upstroke of the radial pulse, features not seen in aortic stenosis.

Comment and Summary

The mechanism controlling transformation of pressure pulse contours during transmission to the peripheral arterial system and the explanation of the amplification of systolic pressure remain obscure. These appear to be related phenomena in the aortic-radial and aortic-femoral systems and are difficult to explain fully by a "standing-wave" hypothesis.[24] It is probable that these phenomena are related to the resonant and damping characteristics of the arterial system.[25,26] In healthy persons, a change of contour between the aorta and the radial artery usually is associated with amplification of systolic pressure at the radial artery. In aortic stenosis and some isolated instances of other conditions (Fig. 9), absence of an increase in systolic pressure at the radial artery is associated with absence of transformation in pulse contour.

In our experience, the reliability of pulse contours for diagnosis has been considerably enhanced by simultaneous recording of central and periph-

eral pressure pulses. Once the mechanism or mechanisms controlling the transformation of pulse contours and the amplification of systolic pressure are known, it is likely that the recording of intra-arterial pressure will become an even sharper diagnostic tool.

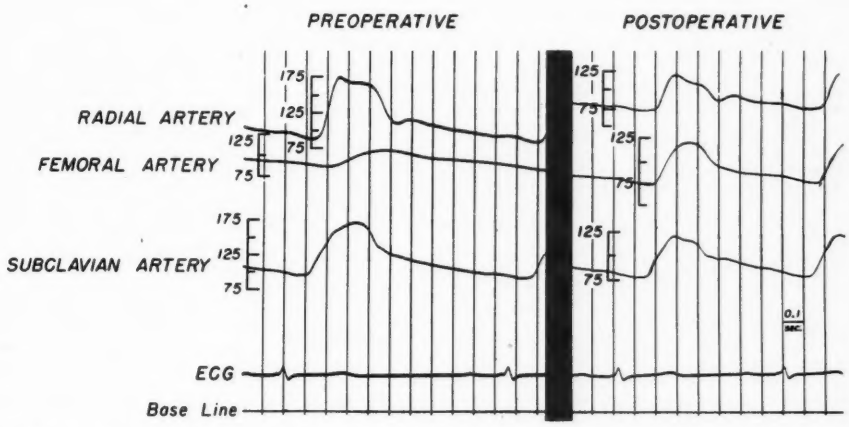


Fig. 8. Comparison of central (subclavian) and peripheral pressure pulses in coarctation of the aorta before and after surgical correction.

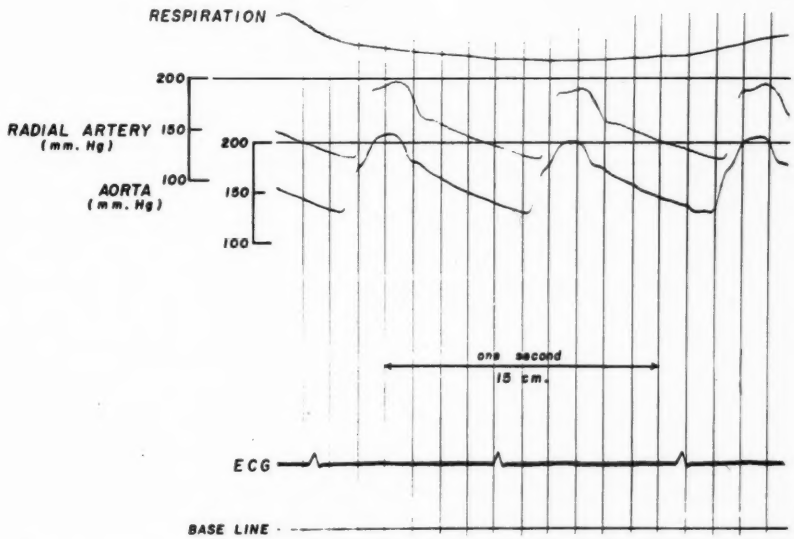


Fig. 9. Simultaneously recorded aortic and radial pulse contours in a nine-year-old boy with systemic hypertension caused by unilateral renal disease. Note the anacrotic radial pulse and absence of an increase in systolic pressure at the radial artery (see text).

References

1. Faivre, Jean: Pathological physiology: Experimental studies on the organic lesions of the heart. In Ruskin, Arthur: Classics in Arterial Hypertension, pp. 67-73. Springfield, Illinois: Charles C Thomas, Publisher, 1956.
2. Frank, O.: Kritik der elastischen Manometer. Ztschr. f. Biol., 44:445-613, 1903.
3. Frank, O.: Ein neues optisches Feder-manometer. Ztschr. f. Biol., 82:49-65, 1924.
4. Wiggers, C. J.: The Pressure Pulses in the Cardiovascular System. New York: Longmans, Green and Co., 1928, 200 pp.
5. Hamilton, W. F., Brewer, G. and Brotman, I.: Pressure pulse contours in intact animal: Analytical description of new high-frequency hypodermic manometer with illustrative curves of simultaneous arterial and intracardiac pressures. Am. J. Physiol., 107:427-435 (Feb.) 1934.

6. Hansen, A. T.: Pressure measurement in the human organism. Acta physiol, scandinav., 19 (suppl. 68):7-226, 1949.
7. Wood, E. H.: Special instrumentation problems encountered in physiological research concerning the heart and circulation in man. Science, 112: 707-715 (Dec. 15) 1950.
8. Dehon, M., Dubus, A. and Heitz, J.: Mesure directe de la pression intra-artérielle chez l'homme vivant: Comparaison avec les procédés cliniques. Compt. rend. Soc. de biol., 72:789-791, 1912.
9. Merke, F. and Müller, A.: Experimentelles zur Hydromechanik und Hämodynamik. V. Blutige Druckmessungen am Tier und am Menschen. Ztschr. f. d. ges. exper. Med., 46:322-370, 1925.
10. Wolf, H. J. and von Bonsdorff, B.: Blutige Messung des absoluten Sphygmogramms beim Menschen. Ztschr. f. d. ges. exper. Med., 79:569-577, 1931.
11. Dameshek, W. and Loman, J.: Direct intra-arterial blood-pressure readings in man. Am. J. Physiol., 101:140-148 (June) 1932.
12. Wood, E. H., Montgomery, G. E., Jr., and Geraci, J. E.: A technique for obtaining multiple arterial blood samples applied to the study of cyanosis in man. Fed. Proc., 7:137 (Mar.) 1948.
13. Wood, E. H.: Symposium on cardiac catheterization: Special techniques of value in cardiac catheterization laboratory. Proc. Staff Meet., Mayo Clin., 28:58-64 (Feb. 11) 1953.
14. Wood, E. H. and Nicholson, J. W., III: A direct reading cuvette oximeter and strain gage manometer assembly for measurement of blood oxygen saturation and continuous recording of arterial pressure and time-concentration curves of Evans blue dye in arterial blood of man. (Abstr.) Am. J. Physiol., 163:762 (Dec.) 1950.
15. Symposium on Diagnostic Applications of Indicator-Dilution Techniques. Proc. Staff Meet., Mayo Clin., 32:463-506 (Sept. 4); 509-553 (Sept. 18) 1957.
16. Hallenbeck, G. A., Wood, E. H. and Clagett, O. T.: Apparatus for recording physiologic variables during operations on man, with observations on changes of blood pressure during resection for coarctation of aorta. S. Clin. North America, 28:851-859 (Aug.) 1948.
17. Thompson, M. C., Patrick, R. T. and Wood, E. H.: Effects of cyclopropane anesthesia on the circulation of human beings. J.A.M.A., 164:389-393 (May 25) 1957.
18. Wright, J. L., Toscano-Barboza, E. and Brandenburg, R. O.: Left ventricular and aortic pressure pulses in aortic valvular disease. Proc. Staff Meet., Mayo Clin., 31:120-126 (Mar. 7) 1956.
19. Wood, E. H., Sutterer, W., Swan, H. J. C. and Helmholz, H. F., Jr.: The technique and special instrumentation problems associated with catheterization of the left side of the heart. Proc. Staff Meet., Mayo Clin., 31:108-115 (Mar. 7) 1956.
20. Wood, E. H.: Physical response requirements of pressure transducers for the reproduction of physiological phenomena: Communications and electronics. Am. Inst. Elec. Eng., No. 23:32-40 (Mar.) 1956.
21. Sutterer, W. F., Swan, H. J. C. and Wood, E. H.: Minimal dynamic response requirements of manometer systems for recording left atrial and ventricular pressures in man. Physiologist, 1:81 (Nov.) 1957.
22. Kroeker, E. J. and Wood, E. H.: Comparison of simultaneously recorded central and peripheral arterial pressure pulses during rest, exercise and tilted position in man. Circulation Res., 3:623-632 (Nov.) 1955.
23. Wright, J. L., Burchell, H. B., Wood, E. H., Hines, E. A., Jr., and Clagett, O. T.: Hemodynamic and clinical appraisal of coarctation four to seven years after resection and end-to-end anastomosis of the aorta. Circulation, 14:800-814 (Nov.) 1956.
24. Remington, J. W. and Wood, E. H.: Formation of peripheral pulse contour in man. J. Appl. Physiol., 9:433-442 (Nov.) 1956.
25. Kroeker, E. J. and Wood, E. H.: Beat-to-beat alterations in relationship of simultaneously recorded central and peripheral arterial pressure pulses during Valsalva-maneuver and prolonged expiration in man. J. Appl. Physiol., 8:483-494 (Mar.) 1956.
26. Warner, H. R.: A study of the mechanism of pressure wave distortion by arterial walls using an electric analog. Circulation Res., 5:79-84 (Jan.) 1957.

STUDY ON HEART DISEASE

Heart attacks strike far more often when a person is resting than when he is working. Approximately 30 per cent of all coronary heart attacks occur when people are resting; a mere 2 per cent when they are engaged in sports, running, lifting or moving a load. Several studies indicate that the highest death rate in men occurs among those employed at sedentary jobs.

Moreover, very few cardiac patients need to curtail their activities drastically. The majority of persons disabled by heart disease recover from attacks to live many years and most are able to resume work. Less than 1 per cent of all victims of heart disease require complete rest.

Studies show that deaths from heart disease tend to rise during the winter months and to decline during the summer.

They further reveal that heart disease takes a far greater toll among men than women—a difference which has been steadily mounting over the past few decades. Thus, within the last forty years, the heart disease death risk within the forty-five to sixty-five-year age group has increased nearly 25 per cent for men and decreased at almost the same rate for women.

Death rates for heart disease vary, too, from state to state, with the New England states heading the list and southwestern states, such as Arizona and New Mexico, ranking last.

As far as classification is concerned, hypertension and arteriosclerosis account for over 90 per cent of deaths for cardiovascular disease, including vascular lesions affecting the central nervous system and myocardium. Coronary heart disease remains the leading heart problem.

However, with adequate care, 22 per cent of patients with heart disease can expect improvement or halting of progress of the disease, compared with only 2 per cent improvement for those without care.

The need for adequate treatment is underscored by the fact that deaths from cardiovascular disease are rising rapidly. The proportion of deaths due to cardiovascular disease has increased from about 20 per cent in 1900 to almost 55 per cent in 1956.

Moreover costs for the disease have been increasing dramatically. They now amount to more than $3 billion worth of working time in the United States, and a loss in income tax to the Federal Government of almost $4 million.—*Patterns of Disease.*

Noninflammatory Diseases of Smaller Arteries and Arterioles

EDGAR A. HINES, JR., M.D.
Rochester, Minnesota

ALTHOUGH the smaller blood vessels constitute a large part of the blood vascular system, there has been little knowledge of or interest in their diseases until relatively recently. Even now the state of the smaller blood vessels in such well-recognized conditions as thromboangiitis obliterans and arteriosclerosis obliterans is largely unknown. Atheromas have been identified in arteries as small as 600 to 1000 microns in diameter. Further study is necessary, however, to determine how widespread these changes are and how important they may be clinically.

It has been shown only recently that changes characteristic of hypertension occur in the cutaneous blood vessels of patients who have essential hypertension and that these changes are similar to those long known to be present in the arterioles of the ocular fundi, pectoral muscles, kidneys and other structures and organs of the body. These changes must be important clinically, since the skin contains such a large part of the smaller blood vessels in the body. In coarctation of the aorta, it has been noted that hypertensive vascular changes are present in the skin, being of equal degree in skin from the calf and from the arm.

A group of diseases clinically different but having somewhat similar histologic changes in the arterioles include acrocyanosis, livedo reticularis, chronic pernio and hypertensive ischemic ulcers of the leg. The predominant histologic changes are varying degrees of arteriolar spasm and sclerosis. The clinical picture is somewhat different in the four diseases. Spontaneous nodular lesions and ulcers may occur in the extremities in all of the conditions. The appearance of the early lesion and its development suggest infarction of the skin, and the ulcer that is produced is of an ischemic type.

These diseases, like Raynaud's disease, occur predominantly in women. The explanation for this is not always clear. Chronic pernio (chronic chilblain) probably occurs more frequently in women because they do not protect their legs adequately from the cold. This also may be the explanation as to why complications are seen more often in women who have livedo reticularis than in men with the same condition. Hypertensive ischemic ulcer occurs mainly in women more than sixty years of age who have moderate to severe hypertensive vascular disease that has been present for many years. One explanation for the predominance of this condition in women is that fewer men than women with severe hypertensive disease live beyond sixty years of age.

Most noninflammatory diseases of the small blood vessels have their predominant clinical manifestations in the skin. When ulceration occurs from infarction, the initial lesion is similar in all. The first abnormality usually observed is a pink or red cutaneous plaque that becomes blue and purpuric within a week or ten days. In most instances, a hemorrhagic bleb develops on the surface of the plaque, and this may break down to form a typical superficial ischemic-appearing ulcer. The surface of the ulcer is usually sensitive and may be extremely painful, especially when it is not covered to prevent drying out of the region.

Acrocyanosis

Acrocyanosis is characterized by persistent blueness and coldness of the extremities, usually of the entire hands and feet. The condition is usually primary (idiopathic), although occasionally it may be seen as a secondary feature associated with signs of pulmonary osteoarthropathy. Trophic changes and gangrene do not occur; ulceration is rare and usually results from local trauma. Because of the pronounced blueness, many patients are concerned by the uncomely appearance and some fear gangrene.

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Treatment.—The condition is usually innocuous and is more annoying than dangerous. In most cases, no treatment is indicated other than a discussion with the patient of the nature of the condition and of the fact that it is not dangerous and is not likely to give any severe disability. In an occasional instance in which the condition is severe, especially when excessive sweating is associated, sympathectomy may be advisable.

Livedo Reticularis

This disorder is characterized by a bluish, reddish, netlike pattern of discoloration that may involve all four extremities; occasionally it occurs over the entire body. The discoloration is permanent, although the intensity may vary with changes in environmental temperature. The color changes and minor discomfort are the only symptoms in about 90 per cent of the patients. The remaining 10 per cent may have disabling chronic ulceration, usually on the lower extremities and most commonly on the lower part of the leg.

Livedo reticularis may be primary and idiopathic or it may be symptomatic of other diseases, such as systemic lupus erythematosus and periarteritis nodosa. In the primary (idiopathic) type, the distribution of the color change is likely to be diffuse and symmetric, whereas the color changes in the symptomatic type are more disseminated and patchy. In most cases, livedo reticularis is not of serious significance. However, it is not rare. About 400 patients in whom this diagnosis was made were seen at the Mayo Clinic during the period between 1945 and 1955. In the symptomatic type, the nature of the underlying disease determines the prognosis.

Treatment.—In mild disease of the idiopathic type, the condition is more alarming than harmful, and reassurance and protection from cold are all that may be indicated. Sympathectomy occasionally may be advisable for those patients who are unable to protect themselves from the cold satisfactorily and who have distressing symptoms of coldness and discomfort when exposed to cold. Two patients at the clinic who had unusual degrees of disability from coldness and paresthesia associated with livedo reticularis that interfered seriously with their occupation obtained great symptomatic relief after sympathectomy. Relief has persisted in these patients for seven and twelve years, respectively.

When ulceration occurs, an initial period of rest in bed is advisable. Local applications of a saturated solution of boric acid or of a 0.5 per cent solution of aluminum subacetate may be of value in clearing up local inflammation in and around the ulcer. Fever therapy by means of the intravenous injection of typhoid vaccine or polysaccharides (pyromen) may be helpful in healing the ulceration. Use of drugs that block the sympathetic nervous system also may be of value. My colleagues and I have used with some success hexamethonium bromide or hexamethonium chloride given subcutaneously in increasing doses up to a maximum of 25 to 40 mg. two or three times daily. We have seen only one patient with livedo reticularis in whom amputation of an extremity was eventually necessary.

Chronic Pernio (Chronic Chilblain)

This is a condition that affects women usually in the fourth or fifth decade of life. Chronic pernio is often unrecognized. The disease is characterized by erythematous ulcerating lesions in the lower extremities, particularly around the ankles and the lower part of the leg. During the earlier stages of the condition, the lesions appear at the onset of cool weather and disappear during the warmer summer months. After the condition has been present for several years, the lesions may appear during the cool days of the summer season. The lesions characteristically go through a cycle in which they develop over a period of two or three weeks and then heal over a period of an additional two or three weeks. The ulcers heal spontaneously, leaving a pigmented and sometimes a depressed scar in the skin. After many recurring crops of lesions, the condition becomes more chronic and extensive chronic changes may be present in the skin of the legs, with pronounced induration and a low-grade inflammatory reaction that is more or less persistent.

Treatment.—The best treatment is prevention. It is important to prevent recurring crops of lesions so as to forestall the chronic indurative stage of the disease in which treatment is extremely difficult and in which it may be impossible to clear up the lesions. Prevention can be accomplished usually by protection from cold and from injury. It may be necessary for the patient to move to a climate that is warmer during the

fall and winter months, one in which the temperature is usually more than 80° F. and the air is dry. Lesions may develop in susceptible patients even though they live in regions ordinarily considered to have relatively mild fall and winter seasons if the temperature goes down during the winter to as low as 50 or 60° F.

When chronic lesions are present that do not clear up spontaneously, the use of vasodilating procedures or drugs may be helpful in eradicating the lesions. The value of sympathectomy in chronic pernio is uncertain. Several of our patients who have had chronic pernio associated with moderately severe hypertension and in whom sympathectomy was done for the hypertension had immediate disappearance of the lesions on the legs. However, recurrence of lesions during subsequent cool or cold weather was not entirely prevented in any of these patients after sympathectomy.

Hypertensive Ischemic Ulcer of the Leg

This is a relatively rare condition. About 100 patients with this condition have been seen at the clinic since it was first described here in 1941. It is usually an unrecognized clinical syndrome. The condition occurs predominantly in women between fifty and seventy years of age. The ulcers may begin spontaneously or may be induced by injury. The lesions most often are located low on the lateral and posterior surfaces of the leg. The ulcers usually are solitary, although injury may induce ulceration in several regions simultaneously. The typical ulcer apparently enlarges by extension of the purpuric hemorrhagic zone into the normal skin surrounding the ulcers. The diameter of the ulcers may range from 1 to 15 cm. The fully developed lesion is often rather painful. The patient may consult a physician more because of the severe pain and disability from pain in the ulcer than from concern about the condition itself. All lesions heal eventually but, if they are not treated, the healing may be extended over many months. In one of our patients, healing did not occur until after a fifteen-month period.

Treatment.—Prevention is also important in the treatment of hypertensive ischemic ulcers of the legs. It is much easier to prevent the initiation of the lesion than to treat it after it has appeared. In the program of prevention, special care of the feet and protection of the feet and legs are of utmost importance. The ankles and legs should be protected especially from minor injury, which is often an initiating factor in the appearance of the lesion.

When an ulcer already is present, it is best to start treatment by a short period of rest in bed, and it may be advisable to keep the patient relatively inactive at least until the ulcer has shown considerable evidence of healing. Appropriate sedative or narcotic drugs are often necessary for control of the severe pain. Local infection may be treated by a saturated solution of boric acid or a solution of antibiotic drugs. The hypertensive ischemic ulcer apparently does not tolerate application of ointments and salves well, and use of such agents should be avoided in most cases. Sympathectomy or the use of one of the sympathetic blocking drugs, such as is given in the treatment of hypertension, may be of help in hastening the healing of the lesion. When the ulcers are large and when the surface of the ulcer is in good condition, skin grafting also may shorten greatly the period of recovery and healing.

MEDICO-LEGAL FILMS AVAILABLE

Seventeen Questions and Answers have been prepared by the Law Department of the American Medical Association and The Wm. S. Merrell Company to supplement "The Medical Witness," a film on medical testimony.

The nine-page Question and Answer folder is available to any physician on request and should be of special interest to program chairman, medico-legal committees and the officers and staff of medical societies. For free copy, write to: Medical Witness Questions and Answers, The Wm. S. Merrell Company, Cincinnati 15, Ohio.

Information about the films, "The Medical Witness" and "The Doctor Defendant," will also be sent on request. These two films are in a series of medico-legal subjects now being filmed by Merrell in co-operation with The American Medical Association and The American Bar Association.

Raynaud's Disease

RAY W. GIFFORD, JR., M.D.
Rochester, Minnesota

FOR MANY YEARS following Raynaud's thesis on local asphyxia and symmetrical gangrene of the extremities,[1] the term "Raynaud's disease" was applied indiscriminately to a variety of conditions which, on close scrutiny and in the light of later knowledge, bore little or no resemblance to the author's original description. It is unfortunate that this early confusion in terminology has left a mistaken impression that persists even today, especially in lay circles where the name "Raynaud's disease" strikes terror and is equated to gangrene and amputation.

Hutchinson[2] was among the first to perceive that Raynaud was describing a symptom and not a single disease. It remained for Allen and Brown[3,4] to bring order out of chaos by carefully reviewing the literature on the subject and clearly defining Raynaud's phenomenon as a symptom of many diseases of which true or primary Raynaud's disease is but one. Just as "all that glitters is not gold," and "all that wheezes is not asthma," so all that blanches is not Raynaud's disease.

Definition of Terms

It is important, therefore, to begin this discussion with a definition of terms.

Raynaud's Phenomenon.—Raynaud's phenomenon results from intermittent episodes of constriction of small arteries or arterioles in the extremities. This is manifested clinically by intermittent changes in color of the skin of the fingers or toes or more rarely the ears, nose, and lips. When the spasm leads to complete occlusion of the affected arteries and arterioles, the skin becomes white. This is the pallor phase of Raynaud's phenomenon. When the spasm leads to incomplete occlusion of the affected arteries and arterioles, the skin becomes cyanotic; this is the cyanotic phase of Raynaud's phenomenon. The episodes of vasospasm may be followed by a period of reactive hyperemia during which the color of the skin becomes excessively red and warm; this is the rubor phase. Some patients with Raynaud's phenomenon may exhibit all three phases of color change. Others may exhibit only the cyanotic phase, and some experience only the pallor phase. The phase of reactive hyperemia or rubor is inconstant, and when it does occur, it follows the episodes of vasospasm. Each phase may last from a few seconds to a few minutes.

Raynaud's Disease.—When Raynaud's phenomenon is primary, that is, when it exists in the absence of diseases or conditions to which it may be secondary, it is called "Raynaud's disease."

This distinction between Raynaud's phenomenon which is a symptom and Raynaud's disease which is a distinct clinical entity is of utmost importance with respect to proper treatment and ultimate prognosis.

Pathophysiology

The pathophysiology underlying the Raynaud's phenomenon is poorly understood. That the intermittent episodes result from spasm of small arteries and arterioles is generally accepted. Whether this predilection to spasm is due to an inherent irritability in the walls of the involved vessel or is due to hyperexcitability of the sympathetic nervous system has not been determined. Organic occlusion of digital arteries does not occur in true Raynaud's disease, although it may be seen when Raynaud's phenomenon is secondary to other conditions. Larger arteries, such as the brachial and its branches, and the popliteal and its branches, are always open in true Raynaud's disease, and this is helpful to the clinician in that demonstration of occlusion of major arteries makes it unlikely that a patient with Raynaud's phenomenon has true Raynaud's disease.

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Diagnosis

In making a diagnosis of Raynaud's disease one must first establish that the patient has *bona fide* Raynaud's phenomenon, for although not all patients with Raynaud's phenomenon have Raynaud's disease, all patients with Raynaud's disease have Raynaud's phenomenon. A carefully taken history usually suffices to establish the presence of Raynaud's phenomenon, but in doubtful cases the vasospastic episodes can frequently be precipitated by having the patient grasp an ice cube or other cold object.

The second step in the diagnosis of Raynaud's disease is to rule out other causes for Raynaud's phenomenon. The diseases and conditions with which Raynaud's phenomenon may be associated are listed in Table I. Raynaud's phenomenon is sometimes the presenting manifestation or symptom of these conditions, and only a detailed history, careful physical examination, and indicated laboratory data will reveal the underlying cause for it. At times the primary disease may escape detection for several months during which Raynaud's phenomenon is the only symptom. Many potentially serious conditions, some of which might result in loss of limb or life, may cause Raynaud's phenomenon (Table I). It is easy to see, therefore, how early writers became confused in their concepts of Raynaud's disease and attributed major amputations and even death to it.

Allen and Brown[3,4] have set forth five criteria for making a diagnosis of true Raynaud's disease. These are (1) Raynaud's phenomenon excited by cold or emotion; (2) bilateral Raynaud's phenomenon; (3) ischemic lesions, when present, limited to small areas of cutaneous gangrene; (4) exclusion of diseases listed in Table I that might be causal, and (5) symptoms for at least two years. Experience has shown that the diagnosis of Raynaud's disease established by adhering to these criteria will be accurate in 95 per cent of cases.[5]

TABLE I. CONDITIONS AND DISEASES TO WHICH RAYNAUD'S PHENOMENON MAY BE SECONDARY

(These must be excluded before a diagnosis of primary Raynaud's disease can be made)

- I. Occlusive arterial disease
  - A. Arteriosclerosis obliterans
  - B. Thromboangiitis obliterans (Buerger's disease)
- II. Systemic diseases
  - A. Scleroderma
  - B. Disseminated lupus erythematosus
  - C. Periarteritis nodosa
  - D. Rheumatoid arthritis
- III. Abnormalities of blood
  - A. Cryoglobulins
  - B. Cold agglutinins
- IV. Intoxication from:
  - A. Lead
  - B. Arsenic
  - C. Ergot
- V. Neurogenic lesions
  - A. Diseases of nervous system
  - B. Thoracic outlet compression (scalenus anticus and hyperabduction syndromes)
- VI. Trauma
  - A. Occupational
    1. Raynaud's phenomenon in typists and pianists
    2. Occupational occlusive arterial diseases of hand
    3. Pneumatic-hammer disease
  - B. Late result of cold injury
    1. Trench foot
    2. Immersion foot
    3. Frostbite

Clinical Characteristics

Raynaud's disease occurs primarily in young women. At the Mayo Clinic 77 per cent of patients with Raynaud's disease are women, and of these women, 78 per cent are less than forty years of age at the time of onset of their disease.[5,6]

The majority of patients state that exposure to cold is the usual stimulus for precipitating Raynaud's phenomenon. Approximately 20 per cent also notice that Raynaud's phenomenon appears under situations of emotional stress, even though the environmental temperature is warm.

Nearly all patients with Raynaud's disease first notice the vasospastic phenomenon in their fingers. Approximately 40 per cent also will have symptoms in their toes. It is unusual for symptoms to appear first in the toes, and even more unusual for symptoms to remain confined to the toes in true Raynaud's disease. Occasionally the vasospastic phenomena of true Raynaud's disease may be unilateral for several years before they become bilateral. However, when unilateral Raynaud's phenomenon is present, one should suspect some local cause, such as occlusive arterial disease, thoracic outlet syndrome, or chronic occupational trauma with occlusion of the palmar arterial arch. Approximately 5 per cent of women with Raynaud's disease will have a family history of Raynaud's phenomenon.

Approximately 10 per cent of women with Raynaud's disease have hypertension (with blood pressure of more than 150 mm. of mercury systolic and 90 mm. diastolic), and approximately 15 per cent have migraine headache. The frequency of functional complaints among women with Raynaud's disease has led Mufson[7] to postulate that in some cases, at least, psychosomatic factors play a prominent role in etiology.

Physical Examination

Complete physical examination is essential in the search for diseases or conditions to which the Raynaud's phenomenon may be secondary.

TABLE II. COMPLICATIONS OF RAYNAUD'S DISEASE AT OR BEFORE FIRST VISIT TO CLINIC FOR 474 WOMEN[5]

Complication	Women	Per Cent
Trophic changes	40	8
Sclerodactylia	34	7
Trophic changes and sclerodactylia	23	5
Calcinosis cutis	1	0.2
Amputation of phalanges	2	0.4

The extremities of patients with uncomplicated Raynaud's disease usually appear normal between vasospastic episodes. Sometimes the hands or feet or both tend to be cool and perspire excessively. Arterial pulsations are palpable at the wrist and in the feet, although an unusually warm environment occasionally is necessary to make them evident.

Special Methods of Investigation

Special procedures such as skin temperature studies, oscillometry, and plethysmography are of little practical value in making the diagnosis of Raynaud's disease. Arteriography is sometimes helpful in ruling out occlusive arterial disease as a cause for Raynaud's phenomenon.

Complications of Raynaud's Disease

Complications of Raynaud's disease occur in less than 30 per cent of cases and are usually not severe. They consist of trophic changes, sclerodactylia, and calcinosis cutis. They may appear separately or together.

Trophic changes occur in the tips of digits and around the nails and include chronic fissures, ulcers, superficial infarcts in the skin, and chronic paronychia. These lesions may heal leaving pitted scars. Extensive gangrene does not occur as a complication of Raynaud's disease.

Sclerodactylia consists of sclerodermatous changes confined to the skin of the fingers. As a complication of Raynaud's disease it never involves more proximal parts and, therefore, can be distinguished from the more extensive involvement seen in diffuse scleroderma and acrosclerosis.

Calcinosis cutis occasionally occurs at the tips of digits of patients who have Raynaud's disease. It appears as tiny globular deposits which may ulcerate and discharge their contents.

The incidence of these complications is not great (Table II). Furthermore, the disability arising from the complications is often minimal. It is surprising, though gratifying, that complications led to amputations for only two (0.4 per cent) of 474 women before or at the first visit to the Mayo Clinic for Raynaud's disease.[5] These amputations were minor, involving only one or more phalanges and were performed for painful and nonhealing ulcers. No major amputations were necessary.

Prognosis in Raynaud's Disease

A recent study has shown that the prognosis for patients with true Raynaud's disease is surprisingly good.[5] Follow-up studies were made on a series of 307 women from three to forty-six years (average seventeen years) after onset of symptoms of Raynaud's disease. None of these women had undergone sympathectomy. Most of them were carefully instructed about protection of their hands from cold and trauma, but otherwise treatment was not standardized, and most patients had not followed any particular therapeutic regimen for prolonged periods.

Ten per cent of the women reported that Raynaud's phenomenon disappeared during the follow-up period; 36 per cent reported that Raynaud's phenomenon had improved. Only 16 per cent reported that Raynaud's phenomenon was worse at the time of follow-up. The remainder noted no particular change in the severity of Raynaud's phenomenon. It is interesting that a detailed study of the smoking habits of these women with Raynaud's disease failed to produce evidence that cigaret smoking had any effect, adverse or otherwise, on the course of Raynaud's phenomenon.

The complications of Raynaud's disease frequently became less troublesome or disappeared entirely. Eighty-seven per cent of the women who had trophic changes of their digits initially had no further ulcerations in the period of follow-up. Sclerodactylia was less noticeable or was causing no disability for 70 per cent of the women who had it initially.

Only 8 per cent of women who were free of the complications of Raynaud's disease when the diagnosis was first made subsequently had trophic changes, sclerodactylia or calcinosis cutis, either singly or in various combinations.

No amputations were necessary for the complications of Raynaud's disease during the period of follow-up.

Twelve (4 per cent) of the 307 women in this group died before the end of the follow-up period. None of the deaths could be attributed to Raynaud's disease or its complications. Indeed, there

is every reason to believe that Raynaud's disease is compatible with a normal life span. But this is not true for secondary Raynaud's phenomenon which may be associated with serious and lethal diseases. For instance, 38 per cent of 98 women with secondary Raynaud's phenomenon who were traced died during a similar follow-up period.[5] The average age at time of death for the women with secondary Raynaud's phenomenon was forty-seven years and 40 per cent were less than forty years of age when they died.

Treatment

Reassurance is the first step in treatment of Raynaud's disease. The physician should first reassure himself that his patient has true Raynaud's disease and that the Raynaud's phenomenon is not secondary to some other disease. He then can confidently reassure his patient and allay the apprehension that arises from misinformation about the nature and prognosis of Raynaud's disease. The patient should be told that major amputation is never necessary for Raynaud's disease and that minor amputations are rarely required.

Protection of the hands and feet from cold and mechanical trauma is important. Cold objects should not be handled without the use of gloves; thus patients with this disease should wear gloves when handling items in the refrigerator or freezer. For going out of doors in cold weather, patients with Raynaud's disease should wear suitable clothing to keep the body as well as the extremities warm. Prolonged immersion of the hands in water as in washing dishes can be harmful, especially when irritating soaps or detergents are used.

Vasodilating drugs such as tolazoline (priscoline) and dibenzyline, or ganglion blocking drugs, such as hexamethonium or mecamylamine (inversine), are sometimes helpful in reducing the frequency of vasospastic episodes. Often, however, such medication is not needed, and in mild cases the side effects which they produce will be more troublesome than the Raynaud's disease. An ointment which contains 2 per cent glyceryl trinitrate applied locally to the involved extremities has proved helpful in some cases.

Surgical sympathectomy should be reserved for those patients whose Raynaud's disease is severe and progressive in spite of adequate medical management. In the experience of my colleagues and me, sympathectomy is necessary for less than 20 per cent of patients with Raynaud's disease.

TABLE III. RESULTS OF SYMPATHECTOMY FOR 70 WOMEN WITH RAYNAUD'S DISEASE[8]

Result	Upper Extremities Denervated		Lower Extremities Denervated	
	Patients	Per Cent	Patients	Per Cent
Excellent	7	10	15	83
Good	30	44	2	11
Fair	6	9	0	
Poor	25	37	1	6
Total	68		18	

Data derived from follow-up study of seventy women with Raynaud's disease who had various types of operations to interrupt the sympathetic nervous pathways prior to 1945 are presented in Table III.[8] The average period of follow-up after operation was twelve years, and in one case it was twenty-eight years. Two patients had operations for the lower extremities only, fifty-two for the upper extremities only, and sixteen, for both the upper and lower extremities.

The results of sympathectomy are consistently better in the lower than the upper extremities, and this striking difference has been reported by other authors.[9-13] All too frequently, sympathectomy for the upper extremities will produce good or excellent initial results, only to be followed by relapse within a few months. The preganglionic thoracic sympathectomy described independently by Smithwick[14] and Telford[15] and the postganglionic cervicothoracic sympathectomy described by Adson[16] produced similar results. There was no operative mortality.

None of these patients had only second thoracic ganglionectomy, and none had the more extensive procedures advocated recently by Ray.[17]

Lest the reader gain the impression that the results of surgical treatment of Raynaud's disease in the upper extremities is little better than conservative treatment, it should be emphasized that only progressive and recalcitrant cases were chosen for such treatment. In other words, most of these patients had failed to respond to medical treatment.

Follow-up studies were conducted also on a group of fifty-four women who had sympathectomy for Raynaud's phenomenon secondary to acrosclerosis, rheumatoid arthritis, occlusive arterial disease, periarteritis nodosa, and other diseases. The results were much worse than in the group with Raynaud's disease. In this series only 20 per cent of women obtained good or excellent benefit from sympathectomy for the upper extremities, and only

50 per cent obtained good or excellent benefit from sympathectomy for the lower extremities. This is another reason why it is so important to differentiate between true Raynaud's disease and secondary Raynaud's phenomenon.

Summary

Raynaud's phenomenon results from intermittent spasm of small arteries and arterioles, usually in the fingers, less often in the toes. It can be associated with and secondary to many unrelated diseases and conditions some of which are serious and even fatal. The prognosis is therefore uncertain until a diagnosis of primary or true Raynaud's disease can be substantiated by ruling out other causes for Raynaud's phenomenon. Raynaud's disease is a benign condition; no mortality is associated with it, and serious disability infrequently results. Raynaud's disease does not lead to extensive gangrene, and major amputations are never necessary. Raynaud's disease is the most common but least serious of the many conditions with which Raynaud's phenomenon may be associated.

Conservative treatment is effective for most patients with Raynaud's disease, but in resistant cases surgical sympathectomy is indicated.

References

1. Raynaud, Maurice: On local asphyxia and symmetrical gangrene of the extremities. (Translated by Thomas Barlow.) In: Selected Monographs, p. 99. London: The New Sydenham Society, 1888.
2. Hutchinson, J.: Raynaud's phenomenon. (Abstr.) M. Press & Circ. n.s., 72:403-405, 1901.
3. Allen, E. V., and Brown, G. E.: Raynaud's disease: Critical review of minimal requisites for diagnosis. Am. J. M. Sc., 183:187-200 (Feb.) 1932.
4. Allen, E. V., and Brown, G. E.: Raynaud's disease affecting men. Ann. Int. Med., 5:1384-1386 (May) 1932.
5. Gifford, R. W., Jr., and Hines, E. A., Jr.: Raynaud's disease among women and girls. Circulation, 16: 1012-1021 (Dec.) 1957.
6. Hines, E. A., Jr., and Christensen, N. A.: Raynaud's disease among men. J.A.M.A., 129:1-4 (Sept. 1) 1945.
7. Mufson, I.: Mechanism and treatment of Raynaud's disease: Psychosomatic disturbance. Ann. Int. Med., 20:228-238 (Feb.) 1944.
8. Gifford, R. W., Jr., Hines, E. A., Jr., and Craig, W. McK.: Sympathectomy for Raynaud's phenomenon: Follow-up study of 70 women with Raynaud's disease and 54 women with secondary Raynaud's phenomenon. Circulation, (In press).
9. Telford, E. D.: Discussion on peripheral vascular lesions. Proc. Roy. Soc. Med., 37:621-624 (Aug.) 1944.
10. Haxton, H. A.: Regeneration after sympathectomy and its effect on Raynaud's disease. Brit. J. Surg., 35:69-76 (July) 1947.
11. Felder, D. A., Simeone, F. A., Linton, R. R., and Welch, C. E.: Evaluation of sympathetic neurectomy in Raynaud's disease, based on follow-up study of 40 patients. Surgery, 26:1014-1033 (Dec.) 1949.
12. Blain, A., III, Coller, F. A., and Carver, G. B.: Raynaud's disease: Study of criteria for prognosis. Surgery, 29:387-397 (Mar.) 1951.
13. Robertson, C. W., and Smithwick, R. H.: Recurrence of vasoconstrictor activity after limb sympathectomy in Raynaud's disease and allied vasomotor states. New England J. Med., 245:317-320 (Aug. 30) 1951.
14. Smithwick, R. H.: Modified dorsal sympathectomy for vascular spasm (Raynaud's disease) of upper extremity: Preliminary report. Ann. Surg., 104: 339-350 (Sept.) 1936.
15. Telford, E. D.: Technique of sympathectomy. Brit. J. Surg., 23:448-450 (Oct.) 1935.
16. Adson, A. W.: Changes in technique of cervicothoracic ganglionectomy and trunk resection. Am. J. Surg., 23:287-288 (Feb.) 1934.
17. Ray, B. S.: Sympathectomy of upper extremity: Evaluation of surgical methods. J. Neurosurg., 10:624-633 (Nov.) 1953.

STORY OF CEREBRAL PALSY

In a booklet just published by the National Society for Crippled Children and Adults, Earl Miers, prominent author, editor and Civil War authority, has written his own story of conquest of cerebral palsy in "Why Did This Have to Happen?"

To assist in solving the perplexing problems which confront parents in raising handicapped children, Mr. Miers offers inspiration. In his moving life story, he points his lesson thus: "I watch two men coming down the street. One propels himself on crutches, the other strides along on a sound pair of legs . . . My eyes cannot tell me which of these two is more severely handicapped . . . I speculate over which is fitter to survive in the specific environment that we share. Which is the more courteous? The more likely to smile? The more aglow with a warmth for life? The more responsive to another's need? The more willing to render faithful service to his employer, his community, his family? Which is better trained in his work and thus more capable of bringing insight and imagination to his labors? Which is less filled with prejudice, less consumed with deceit?"

He goes on to say: "Judge and musician, innkeeper and statesman, actor and surgeon—each endures by holding onto beliefs. For any person possessing firm foundations of intellectual strength and spiritual stamina, legs that wobble or arms that shake constitute inconsequential handicaps. As long as any man has a right to be born, a purpose to fill on earth, then a crippled child holds the same right, the same purpose."

The booklet, which is one of a series designed to help parents of crippled children, is available at the nominal charge of 25 cents from the National Society for Crippled Children and Adults, 11 South La Salle Street, Chicago 3, Illinois.

Periarteritis Nodosa and Temporal Arteritis

RICHARD M. SHICK, M.D.
Rochester, Minnesota

PERIARTERITIS NODOSA is a disseminated disease of unknown origin characterized by focal inflammatory lesions which involve chiefly medium-size and small arteries and arterioles. It has been classified as a so-called collagen disease, and as such takes its place with other rheumatic and "pararheumatic" syndromes as an inflammatory and degenerative disease of the connective-tissue system.

Incidence.—The incidence of this disease is somewhat higher among males than among females. It can occur at all ages, but a majority of the patients are between the ages of twenty and forty years.

Etiologic Aspects.—As is true of all obscure conditions, many opinions as to cause have been advanced but none has been satisfactorily confirmed or completely accepted.

Present opinion is that multiple etiologic factors may be involved in the production of the disease, with a sensitivity reaction to either drugs or infectious processes playing a prominent role.

Pathologic Aspects.—The pathologic pattern consists of a primary injury to the wall of the vessel, with necrosis of the media, destruction of the internal elastic membrane and infiltration of the adventitia by polymorphonuclear leukocytes, many of which may be eosinophils. Aneurysms occur in probably less than 20 per cent of cases. Occasionally these may rupture. When the process extends to the intima, the smaller vessels frequently become occluded. Characteristically, arterial lesions in any and all stages of activity are present at the same time. At necropsy, rarely, all the lesions are healed.

Symptoms and Signs.—The symptoms and signs are protean. They may vary from time to time and this variation may produce a most confusing clinical picture. They depend entirely upon the stage of the disease and the organs or tissues involved. In general, periarteritis nodosa creates the impression of an infectious disease with toxemia. Frequently, it is characterized by cachexia associated with malaise, anorexia and low-grade fever, with additional symptoms and signs referable to the organs and tissues affected.

The renal manifestations usually are those of nephrosclerosis or glomerulonephritis. Hypertension is a frequent finding, and usually it is associated with vascular and other changes in the kidneys. At times, it is difficult to distinguish periarteritis nodosa from malignant hypertension.

Many of the patients die in uremia, but the only signs of renal involvement may be microhematuria or albuminuria.

Abdominal pain is one of the common early symptoms. Hepatomegaly and jaundice may occur, but usually are not pronounced. Complications, such as perforation of a gastric or intestinal ulcer, infarction of the bowel or necrosis of the pancreas, may develop and the diagnosis may be established at exploratory laparotomy.

Tachycardia is common. Electrocardiographic changes usually are nonspecific and variable. "Strain" patterns may be noted in patients with hypertension. Although anginal pain is uncommon, myocardial infarctions often are found at necropsy. Pericarditis may occur, and cardiac failure is a common terminal manifestation of the disease.

The most common pulmonary manifestations are wheezing, dyspnea and cough. These symptoms may be secondary to either asthma or heart failure. The incidence of asthma in periarteritis nodosa probably is less than 25 per cent. Hemoptysis, due to infarction or rupture of an involved vessel, may occur. Pleuritis with pleural effusion secondary to pneumonitis or infarction is not uncommon. The roentgenogram of the thorax may

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

show no specific changes. A fanlike pulmonary infiltration extending out from the hilar region, although not pathognomonic of this disease, may suggest the diagnosis in an otherwise obscure problem. Loeffler's syndrome may be a variant of the disease, confined to the lungs, from which recovery occurs, in most instances. Terminal bronchopneumonia frequently is the immediate cause of death.

We have noted overt clinical evidence of involvement of peripheral nerves in approximately 50 per cent of our cases. As a rule, such involvement is of the mononeuritis multiplex type, with asymmetric involvement of single nerves. Scotomas, blurring of vision and paresis of extraocular muscles may occur. The ocular fundi may exhibit typical vascular lesions in the choroid and retina, retinal detachment or hypertensive retinopathy. Cerebral hemorrhage as the result of hypertension, infarction or rupture of an involved vessel is an occasional cause of death.

Symptoms in the joints are noted frequently; they may vary from transitory arthralgia to migratory arthritis. Muscular pain and soreness are common. Osteoporosis may occur. We have encountered aseptic necrosis of the hips in one of our cases. The coexistence of periarteritis nodosa with other rheumatic and "pararheumatic" diseases has been observed by us and by others.

The endocrine organs most often involved are the adrenal glands, pancreas and testes.

Many types of lesions of the skin have been described, including erythema, scarlatiniforme, petechial, purpuric, maculopapular, urticarial and vesicular eruptions, livedo reticularis, subcutaneous nodules and cutaneous infarction with necrosis and ulceration. A special cutaneous form of the disease has been described as "periarteritis nodosa cutis." This usually is unaccompanied by systemic manifestations, and appears to have a benign course.

Laboratory Aspects.—Laboratory findings for the most part are nonspecific. Moderate to marked leukocytosis may be present. Eosinophilia is inconstant; it occurs in less than 20 per cent of cases. The erythocyte sedimentation rate invariably is rapid during the active phase of the disease; values of more than 100 mm. in 1 hour (Westergren) are not uncommon. Secondary anemia often is present; it may be mild to severe. The association of acquired hemolytic anemia and platelet thrombosis with periarteritis nodosa has been reported. Biologic falsely positive serologic reactions to tests for syphilis and increased values for plasma globulin may be obtained. Porphyrinuria has been noted when the liver is involved. Hematuria, albuminuria and cylindruria are common.

Clinical Diagnosis.—The disease should be suspected in a patient who has an obscure type of illness characterized by fever, progressive decline of general health, and the symptoms and signs of a diffuse systemic process, with involvement of several organs and tissues, particularly the kidneys, gastrointestinal tract and peripheral nerves. The presence of a rapid sedimentation rate, leukocytosis with or without eosinophilia, asthma and hypertension, and failure of the condition to respond to conventional treatment make the diagnosis even more likely. In the final analysis, however, a definite diagnosis can be established only by histologic examination. A positive result of biopsy is the best diagnostic evidence of the disease, but a negative result does not exclude the diagnosis.

Prognosis.—In general the prognosis is poor. However, a few spontaneous recoveries have been reported. Spontaneous recovery may be expected under the following circumstances: confinement of the disease predominantly to nonvital structures, minimal involvement of organs followed by healing, and localization of the disease to part of a single organ.

Treatment.—Until the introduction of cortisone and related steroids, there was no specific treatment which would either prevent or alter the course of periarteritis nodosa.

We have administered cortisone or related steroids to approximately fifty patients with periarteritis nodosa. Follow-up data have been obtained in thirty cases in which cortisone or corticotropin was used. Clinical diagnoses were confirmed by biopsy in all cases. Doses of each hormone were initiated at fairly high levels, and were regulated according to the patient's response. In general, 300 mg. of cortisone was administered on the first day and 150 to 200 mg. was given daily thereafter for six weeks. The dose was then gradually altered by decrements of 12.5 to 25 mg. every three or four days, and treatment was dis-

continued in most instances after three to four weeks. We prefer the intramuscular route of administration of cortisone, at least during the initial six weeks of treatment. Our clinical impression has been that the results are more favorable and the incidence of relapses after cessation of therapy is less when the intramuscular route is employed than when the oral route is used. The reason for this is not clear, but it may be associated with a greater cumulative effect of the drug obtained by the intramuscular route as opposed to the oral route. The dose of corticotropin was one-third to one-half that of cortisone.

Additional measures included restriction of sodium in the diet and the administration of potassium chloride in doses of 3 to 6 gm. a day to patients with adequate renal function. Some patients required more than one course of treatment, and in a few instances it was necessary to continue suppressive therapy with orally administered cortisone in doses of 25 to 75 mg. daily.

Clinical phenomena that followed the administration of cortisone and corticotropin in these cases include: (1) prompt subjective relief, (2) subsidence of fever in most cases within twenty-four to seventy-two hours, (3) gradual decrease of sedimentation rates to normal, (4) partial relapses among some patients after withdrawal of the use of the hormones, and (5) improvement in these patients after treatment was resumed. Despite initial improvement, six patients died shortly after treatment was instituted or soon after administration of the hormones was discontinued. In two of these cases necropsy revealed evidence of complete healing of all arterial lesions. In the process of healing, fibrous obliteration of the lumens of the involved vessels had occurred, resulting in widespread visceral infarction.

In the other four cases, necropsy showed widely disseminated arterial lesions in all stages of activity, with multiple visceral infarctions. Three other patients died—four, twenty and thirty months, respectively, after treatment. These patients died elsewhere, and postmortem examinations were not performed. Although adequate information was unobtainable, death was presumed to be the result of irreversible effects of the disease. The disease of the remaining twenty-one patients appeared to be either in remission or adequately suppressed when they were last observed after intervals ranging from one year to five years after the initial course of treatment. However, in most instances, evidence of some residual vascular damage had persisted.

Conclusions.—It appears that cortisone and corticotropin can induce clinical remissions *in* or suppress activity *of* periarteritis nodosa in some cases, and that they may alter effectively the primary pathologic process. Treatment should be instituted early, before widespread vascular damage has occurred, and should be intensive and prolonged. The suppressive effects of prednisone and prednisolone appear to be comparable to those of cortisone administered by the oral route.

Temporal Arteritis

Temporal (cranial) arteritis is a clinical and pathologic entity that occurs in elderly persons. It is characterized by symptoms and signs referable to inflammation of the temporal arteries, by constitutional effects suggestive of a low-grade subacute or chronic infectious process and by histologic evidence of a granulomatous arteritis of the affected vessels.

Etiologic Aspects.—The cause of temporal arteritis is unknown.

Incidence.—In practically all the reported cases the patients have been more than fifty-five years old, and most of them have been more than sixty-five years old. The incidence according to sex is about equal.

Pathologic Aspects.—The disease affects isolated segments of the temporal arteries and occasionally other arteries, especially branches of the carotid arteries. Grossly, the affected arteries are larger than normal, and may be nodular. Frequently they appear to be solid cords with little or no lumens. Histologically, there is usually narrowing or complete occlusion of the lumen produced by intimal proliferation, with or without thrombosis. There are definite but rather localized periarteritis and mesarteritis. Generally, one sees focal necrosis of the media and replacement with gramulomatous tissue containing numerous foreign-body giant cells. Eosinophilic infiltration is uncommon and aneurysmal dilatations are rare.

Symptoms and Signs.—The onset of the disease may be insidious or sudden, and the course is that of a subacute or chronic infection, with local and

systemic manifestations. Local manifestations include severe, throbbing headache with tenderness, swelling and induration of the temporal and occasionally the occipital arteries. Often there are erythema of the overlying skin and pain in the adjacent structures, such as the scalp, face, eyes and jaws. The lesions may begin on one side of the head, but as a rule the arteries on both sides ultimately become involved. Early in the course of the disease, the affected arteries may pulsate, but later the pulsations may disappear.

Generally, a systemic reaction is present, with low-grade fever, malaise, muscular aching, anorexia and loss of weight. These may occur a few weeks or even a few months before the local signs become apparent.

Laboratory Aspects.—Laboratory findings are constant but nonspecific. Mild anemia and mild to moderate leukocytosis usually are present. The sedimentation rate is invariably rapid during the active phase of the disease, generally exceeding 100 mm. in 1 hour; normal or only slightly increased values make the diagnosis impossible.

Clinical Diagnosis.—Ocular involvement occurs in more than 50 per cent of the cases. Involvement of the eyes usually is due to occlusion of the central retinal artery or branch arterioles or to ischemic optic neuritis, and it may result in partial or complete loss of vision in one eye or both eyes. The eyes may become involved within a few days or as late as several months after the onset of the disease. In general, however, ocular symptoms begin within three to six weeks after the onset of headache and after a somewhat shorter interval following the appearance of induration and tenderness of the temporal arteries.

Loss of vision may occur suddenly or slowly over a period of several weeks. The symptoms may vary from blurring of vision and different patterns of defects in the visual fields to complete blindness. More than a third of the patients whose eyes are involved lose their sight permanently, and only a few regain normal vision. Paresis of extraocular muscles may occur. We believe that this paralysis is caused by ischemia of the extraocular muscles resulting from involvement of the muscular branches of the ophthalmic artery, and we think it may be transient.

Cerebral complications have been reported, but are uncommon. Sudden complete deafness has been noted, and in one of our cases the radial arteries were affected by the same pathologic process as the temporal arteries.

As a rule, it is not difficult to make the diagnosis if the possibility of temporal arteritis is kept in mind whenever an elderly patient complains of pain and soreness in the temporal region. We know of no other condition in which localized tenderness and induration are felt along the course of the temporal arteries. An elderly patient who has transitory amblyopia or sudden loss of vision should be carefully examined for tender, indurated or pulseless temporal or occipital arteries, and the symptoms should be reviewed from the standpoint of possible temporal arteritis. A rapid sedimentation rate invariably is present during the active phase of the disease. When the diagnosis is doubtful, it may be confirmed by biopsy of what appears to be an involved vessel.

Generally, the disease runs a self-limited course, lasting from two to thirty months, with an average duration of about six months. The active and symptomatic phase gradually subsides, although occlusion of the involved arteries may persist. Relapses may occur but are uncommon.

Although temporal arteritis usually is a benign and self-limited disease, a mortality rate of 12.5 per cent has been reported, deaths having been attributed to cerebral thromboses and disseminated arteritis, histologically similar to that in the temporal arteries. This is contrary to our observations in a comparable series of cases in which there were no deaths.

Treatment.—Until the advent of cortisone and related steroids the treatment of temporal arteritis was mainly symptomatic, consisting of the usual measures to relieve pain. Excision of a portion of the involved segment of the artery generally relieves the pain of local origin but seldom, if ever, has any effect on the general manifestations or the course of the disease. Roentgen-ray irradiation of the affected arteries and the periarterial injection of procaine hydrochloride likewise may relieve the local distress.

We have administered cortisone or related steroids to approximately seventy-five patients with temporal arteritis. Clinical diagnoses were confirmed by biopsy in most cases. We have recently reviewed fifty-five cases in which the diagnosis was proved by biopsy; we did this to evaluate the effect of steroid therapy. In general, the dose

schedules were essentially the same as for patients with periarteritis nodosa. There appears to be little advantage in the parenteral over the oral route of administration of cortisone in this disease. In some instances, it was necessary to continue suppressive treatment with orally administered cortisone in doses of 25 to 75 mg. daily until the disease had completed its natural course.

Since we believe that in respects other than ocular, temporal arteritis is primarily a self-limited and benign condition, prevention and treatment of the associated visual loss are of paramount importance. All but a very few patients in this series were promptly relieved of their other symptoms by the administration of adrenal corticosteroid.

Thirty-one (56 per cent) of the fifty-five patients, at the time of admission to the clinic, had ocular involvement which was considered to be part of the syndrome of temporal arteritis. Twenty patients (36 per cent of the group) had some loss of vision at the time of admission, and one patient had transient amblyopia after the institution of hormonal therapy. In this group of twenty patients, six had unilateral blindness and five had bilateral blindness. The condition of none of the blind eyes improved under treatment. However, bilateral blindness did not develop in any patient during treatment. The percentage of occurrence of bilateral blindness increased from six on admission to seventeen at the time of discharge in a previous group of fifty-three patients with temporal arteritis seen at the clinic prior to the introduction of steroid therapy.

Total blindness and long-standing partial loss of vision are unlikely to abate with any type of treatment. When loss of vision is partial and of recent onset, some restoration of vision may occur, with or without treatment.

That the hormones promote histologic healing is subject to question, since follow-up biopsies in several of these cases revealed little more healing of the arterial lesions than would be expected in the natural course of the disease.

In the past we have not routinely administered anticoagulant agents to patients with temporal arteritis. We feel, however, that the combined use of anticoagulants and adrenal corticosteroids might be indicated and might be of value in certain instances, notably for patients who have had recent impairment or loss of vision in one eye. It is conceivable that in such cases inflammatory changes already may have developed in the ophthalmic artery of the presumably uninvolved eye, and that subsequent occlusion with loss of vision may supervene, with or without steroid therapy. The intermittent inhalation of 100 per cent oxygen has seemed to be of some benefit in cases of acute or recent visual impairment, but we have not been impressed with the value of vasodilating drugs or stellate-ganglion blocks in such cases.

Conclusions.—The chief value of adrenal corticosteroids in the treatment of temporal arteritis is to suppress the arteritis as long as it endures, and thus to safeguard the degree of vision which remains.

THERAPY OF TOYS IN CHILD'S PLAY

Dr. Grace Langdon, one of the country's well-known leaders in the field of child development and specialist in the relation of toys to everyday living, has written a booklet entitled "Your Child's Play," which was recently released as one of a series of booklets to be published by the National Society for Crippled Children and Adults as aids to parents of crippled children.

Dr. Langdon in her booklet points out that all children, whether crippled or not, live through play, and she offers guidance in play interests, materials, and facilities as well as friends with which to share them.

She says, "Play is much more than filling in time when a child has nothing to do. Through play a child investigates, explores, experiments, discovers. He learns the feel of things. He discovers what he can do with them. . . . He notices the motion of things around him, and with hands, arms, legs, joins in this movement through feeling its rhythm. . . . As a child plays he put his ideas and feelings into action. He finds out what will work and what will not. He picks up new ideas and tries them out. He enjoys, thinks, feels, lives through his play."

Twenty-two additional booklets, two more scheduled for publication in 1958, will comprise the Parent Education series as it is presently planned. These will be on subjects such as the young child in the family, orthopedic handicapipng conditions, problems of adolescence, and emotional growth in parents.

Purposes of the series, as set forth by Dean W. Roberts, M.D., executive director of the National Society, are to offer guidance to parents in creating an abundant and satisfying life experience for themselves and their children; to dispel feelings of loneliness and helplessness in facing problems of growth and development; to provide a medium through which the parent may grow with his child, and to give insight through competent information.

The booklets are available at the nominal charge of 25 cents each from the National Society for Crippled Children and Adults, 11 South LaSalle Street, Chicago 3, Illinois.

Peripheral Vascular Diseases

Evaluation of Treatment

EDGAR V. ALLEN, M.D.

Rochester, Minnesota

THIS PRESENTATION should more appropriately be entitled "An Excursion into Skepticism," for one needs much critical evaluation to keep an even scientific keel in a world in which claims for the value of various treatments are so common and evidence for such value is so sparse. The way of the skeptic is hard. Popularity contests are not won by seekers after truth. Yet skepticism, I believe, needs no defense, whereas credulity simply has no defense.

The history of all fields of human endeavor indicates that progress can be made only when people are dissatisfied with the current situation. Almost all research programs are predicated on beliefs that what is commonly accepted is false or inadequate. Inasmuch as this is the three hundredth anniversary of the death of William Harvey, who was one of the greatest proponents of objectivity in medicine, I may appropriately quote a small part from his perceptive writings. He stated: "I learned and taught anatomy not from books but from dissections, not from the position of philosophers but from the fabric of nature."

Criticism of Present Handling of Pharmaceuticals

To each of you almost every day comes printed material from pharmaceutical firms, which, if entirely true, would simplify the practice of medicine and improve the mental and physical health of almost everyone who is ill. I have been told that one pharmaceutical firm makes several hundred products which are marketed largely because physicians prescribe them or because people buy them without prescription. A physician has reported that he receives more than 2,000 pieces of advertising literature annually. The *Physicians' Desk Reference* for 1958 devotes 138 pages to listing about 27,000 "therapeutic items." The yearly bill for drugs includes these production and promotion costs, and profits for manufacturer and distributor as well. It is enormous, and I am sure that some of the money could be spent in a much better cause—for example, research.

If I have spoken critically of pharmaceutical firms, I have done so with the full knowledge that some are interested more in profit than in honesty. They must, of course, operate within existing laws, but such laws are woefully inadequate. I shudder every time I see the advertisements on television for such products as bufferin and anacin, and I remain eternally curious that such exaggerated claims are permitted. Although the fault lies chiefly with inadequate control, it is well for all of us to know that some of the shabby and dishonest presentation rubs off on physicians because the public cannot differentiate between the medical profession and a pharmaceutical firm. I am aware that many pharmaceutical firms have contributed greatly to scientific advancement by way of better drugs, but I lament the dilution of the virtues of many with the faults which proceed from the desire for great profit on the part of some.

Still I cannot leave the subject with a simple indictment of pharmaceutical firms. I have implied already that ordinarily a medicine cannot be marketed satisfactorily without the co-operation of many physicians who exhibit an amazing credulity. There seems to be common a naive belief that whatever is written is true. And for another reason I cannot restrict my criticism to pharmaceutical firms alone: in many instances the allegations as to the benefits of a preparation are based on studies reported by physicians who have no official association with pharmaceutical firms. I do not know the complete explanation for this situation, but it appears to represent lack of knowledge of the requisites for a scientific study on one hand and a desire to publish positive

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

results on the other hand. There seems to be much more credit in establishing virtues for a product than in determining that a preparation has no virtue.

I feel compelled to say a few words concerning the attitude of editors of medical journals. They may publish articles from those of us who are not particularly skilled in consideration of this subject; too often they do not refer such articles to experts for evaluation. Moreover, some medical journals accept advertisements with little or no regard for the virtue of the product which they advertise. It is my firm belief that the editors of medical journals should accept advertising only for products which they know have virtue.

Underlying the total problem which I have discussed briefly is the desire to assert the positive view, the desire to believe the positive assertion, which sways editors, physicians, and people at large. Hardly any patient wishes to disappoint his physician with an unfavorable report. This situation can be handled best by the "double blind" test in which neither the patient nor the physician knows whether the patient is receiving a medicine or a placebo. The general lack of favor for this approach is an indication that physicians do not care to take trouble in finding the truth or that indeed they do not want to know the truth.

Over a period of years I have been asked to test this and that. When I have agreed, I have frequently been disappointed, for the results of study have usually indicated that a preparation had no virtue or much less virtue than I had anticipated on the basis of prior information.

Recommendations.—I know that one should never be wholly destructive in criticism. Because of this and the seriousness of the problem, I wish to make suggestions for an aggressive approach to the solution of it.

1. All pharmaceutical firms should voluntarily abstain from exaggerated advertising. (Such firms, of course, do not now adhere to the same policy in this regard.) I have little or no hope that this gratifying change will be accomplished, although any pharmaceutical firm which carried out such a policy would certainly endear itself to many physicians. There is, however, the problem of dividends and capital gains.

2. There should be control of advertising to restrict it to just and valid claims. Here again I see little reason for optimism. What would become of our television programs if people knew that bufferin is only aspirin plus a couple of antacids, and that anacin is only acetophenetidin with aspirin and caffeine added? In my opinion much of the television programming is of such a low order that I hope many of them will disappear. Unfortunately people might be forced into conversation or reading, both of which appear to be becoming increasingly painful.

3. For a period of one year, physicians without the ability of perceptive evaluation should throw all advertisements into the waste basket and refuse to converse with "detail men." There is a little danger in such a program, which could be avoided if a medical periodical such as the *Journal of the American Medical Association* would publish immediately any important discovery. In this third recommendation, I am wholly pessimistic; the pictures are so pretty!

4. Medical editors should refuse to publish articles which do not have the approval of experts. This actually is possible, although I fear many experts are too busy. One of my colleagues has mentioned "freedom of the press" in this regard. If this is an issue, and unprepossessing papers must be taken, then the editors should encourage publication of rebuttals.

5. Medical editors should accept advertising of only those products which have proved value. My pessimism deepens; medical journals would undoubtedly be more costly and physicians would object. Who wants to pay fifteen to twenty-five dollars for a medical journal of twelve—or fifty-two—issues annually? Of course a ticket to a popular Broadway musical might cost as much, but there is a difference between fun and education even when one is brief and the other enduring.

6. I conclude reluctantly that my five suggestions are almost wholly impractical. This brings me to a sixth suggestion which is perhaps more palatable because it leaves decision to someone else: namely, a national testing laboratory. Inasmuch as this meeting is under the auspices of the Minnesota Heart Association, an affiliate of the American Heart Association, I will restrict my remarks to the problem of evaluation of drugs alleged to be of value in the treatment of patients with cardiovascular diseases. This situation represents only a small part of the whole; but if such a laboratory were established and maintained by the American Heart Association, its orderly investiga-

tions might persuade appropriate organizations to follow a similar program. I refer to representative bodies in the fields of nutrition, psychiatry, neurology, and gastroenterology, for example.

Such a program of study would be well within the stated objectives of the American Heart Association. It would require indefinite tenure for investigators to protect them against the actions which might arise from disdain and hostility. It would require good scientific minds dedicated to the principle that a negative result is as good as a positive one. The results achieved would certainly protect the public in general and physicians specifically against poor investments in drugs. I suspect it would find little attractiveness for those qualified for such study, but perhaps there is enough missionary zeal in the United States to make possible the implementation of such a program. An agency other than the American Heart Association is currently establishing such a program.

Now I abandon an introduction which has threatened to swallow the entire presentation and return to the specific subject which has been assigned to me.

Atherosclerosis

The most important peripheral vascular disease is atherosclerosis. The idea that man is a composite of that which he eats is certainly not new. Actually, the idea is an obvious expression of ignorance. However, the proposition that atherosclerosis is a manifestation of the fat which man eats must be considered. Almost all of you know that this idea is based on the observation that atheromatosis can be produced in some animals by feeding them excessive amounts of cholesterol and fats. It has seemed a relatively easy transition from experiments on animals to conclusions relative to man.

Too little consideration has been given to the fact that patients eating essentially the same diet become ill and die in diverse ways and periods of life. One may question why my mother died of acute myocardial infarction at the age of forty-eight and why my father has no clinical evidence of atherosclerosis at the age of ninety-two. A study of ancestors and siblings in this instance reveals clearly a genetic factor of great importance. Also, no one has explained satisfactorily to me why atherosclerosis involves the coronary and cerebral arteries and those of the legs, while it leaves unaffected the pulmonary arteries and those in the upper extremities.

But even within the scope of the experiments so widely reverenced, a fundamental omission exists. In applying the findings in animals to the problem in man there has been, for the most part, neglect of the observation that arterial occlusion, which may be a grave complication of atherosclerosis, almost never occurs in the animals in which atheromatosis has been induced. This provokes an important question as to whether or not benign atheromatosis of animals is the equivalent, in an etiologic way, to complicated atheromatosis of man. I do not know the answer to this question, but as of this date I see no significant evidence that it is "yes." I cannot recommend a low-fat diet for everyone in September, 1957.

I can recommend that attempts be made to reduce the concentration of fats in the blood when they are persistently and significantly increased in amount, although even in this situation there is more presumption of a causal association than evidence of it. Hardly anyone likes to restrict or modify his diet; hence I suggest beginning with the ingestion of nicotinic acid in the amount of 500 mg. six times daily. The anticipated flush is seldom troublesome after the first few doses of nicotinic acid, and many times the concentration of fats in the blood is reduced. If the administration of nicotinic acid fails to reduce the fat in the blood in four weeks, it may be replaced by administration of one of the plant sterols, such as sitosterol. If this is ineffective in a period of several weeks, it too may be abandoned.

We arrive now at consideration of the use of unsaturated fats such as safflower oil or corn oil, which needs more study. I anticipate a flood of literature on the use of unsaturated fats; indeed, the flood seems already here. It is clear that there have been and will be exaggerated claims. I have before me an advertisement for linodoxine emulsion which reads as follows: "Useful prophylactically or therapeutically in patients who either show elevation of serum cholesterol or fall into one or more of the following clinical categories: male patients with precordial pain; overweight middle-aged patients of both sexes; patients with visibly tortuous superficial arteries; patients with elevated blood pressure." This statement is for the most part pure nonsense. It is calculated to assure the widest possible use of linodoxine emulsion regardless of need. I certainly will

abstain from the use of it. The advertisement should insult the intelligence of every physician, but it has much in common with material which comes to you repeatedly.

Nevertheless, I do believe the trial use of unsaturated fats has a place in an attempt to reduce the concentration of cholesterol in the blood when the increased value persists despite the countermeasures mentioned previously.

A final measure which may be effective in reducing the amount of fat in the blood is a diet restricted in fat to about 30 grams. Among patients, the respect for such a diet varies widely —from complete adherence to complete negligence. This is a situation commonly noted in attempts at reduction of weight by means of diet. I have a simple philosophy in this regard: the major function of a physician is to recommend; it does not include police responsibility.

Hypertension

The next most important peripheral vascular disease is hypertension. When this is a significant problem, original studies should include the search for pheochromocytoma, aldosteronism, coarctation of the aorta, and unilateral renal disease. The treatment of essential hypertension is very satisfactory, although active preparations used to correct hypertension have other effects besides reduction of blood pressure. I have observed lupus erythematosus and rheumatoid arthritis from hydralazine (apresoline), mental depression from rauwolfia, and psychosis from mecamylamine (inversine). These and other reactions, however, are far from sufficient to justify avoidance of the use of these drugs. Incidentally, I believe that apresoline, the various rauwolfia preparations, and the ganglion-blocking agents are the only drugs which are satisfactory in the treatment of chronic essential hypertension.

But for the past five years, my chief concern regarding hypertension has been the failure of physicians to appreciate the need for treatment. Too often they delay action until distressing complications have developed, or they permit patients to abandon a regimen of treatment which has been established. There is common agreement that patients who have hypertension with retinopathy or with papilledema need treatment, and studies show sharply reduced mortality as a result of adequate measures. It is about the need for treatment of patients with uncomplicated hypertension that disagreement lingers. My own opinion may be simply stated: Hypertension is an abnormal condition which is a notorious provoker of atheromatosis; it should be treated. On a number of occasions when I have participated in panels dealing with hypertension, some physician has disagreed with my opinion. I have always asked him whether he would prefer to have hypertension or normal blood pressure; he has always replied that he would prefer to have normal blood pressure if he had no significant side reactions from drugs. I have never been quite certain of the reason for a physician's desiring to have normal blood pressure when he did not believe his patient needed to have it.

I will turn from these brief remarks upon essential hypertension with the statement that of course there should be continuing study to determine the cause of this disease.

Arterial Occlusion and Aneurysm

The third most common peripheral vascular disease is comprised of complications of atherosclerosis, namely arterial occlusion and aneurysm. The prognosis for untreated aneurysm is so grim that operation is logically advisable. I bow with respect to my surgical colleagues who have accomplished so much in this field. For the most part, aneurysm is a disease of the aged who have atherosclerosis in other areas. This situation and the inherent risk of operation which is present, without reference to age, promote a surgical mortality which is substantial. However, the risk of operation is less than the risk of withholding surgical treatment in most instances. Some patients who believe their lives have almost reached a full cycle prefer the risk of going without surgical treatment; their opinions are to be respected if they are based on complete information.

You will hear much during this program relative to re-establishment of circulation in cases of segmental occlusion of the abdominal aorta or the iliac or femoral arteries. Here, again, I observe a remarkable example of the great skill of surgeons and I am gladdened at the immediate results, which are extremely good in most instances. All of us who participate in this field of medicine are aware that a surgeon cannot cure atherosclerosis. He may, however, correct an impediment to the flow of blood, an accomplishment which is gratifying to patient and physician alike. We have noted on occasion that, at a variable

period following operation, such patients may have angina pectoris, acute myocardial infarction, or cerebral arterial insufficiency, which may be lethal or of grave importance. In considering operations for occlusion of the abdominal aorta, the physician must measure the operative and postoperative risk against the degree of current disability; and the patient should share in this evaluation.

Anticoagulants, such as heparin and dicumarol and drugs having similar action, have achieved an established place in the treatment of vascular disease. Part of this situation is owing to sound observation and part to sound theoretical considerations. In substantial degree, we lack satisfying evidence of their value, based on case-matching. The difficulty in obtaining this is great, because of the infrequency of finding two patients who have exactly similar diseases.

I am concerned particularly about the use of dicumarol and drugs of similar action. Our first report on the use of dicumarol was published in 1942, and during the fifteen years which have elapsed, a multitude of reports have been published and presented orally. Still I must regretfully say that many physicians remain uninformed about, and many laboratories remain unable to report accurately on, prothrombin activity. Consequently the prothrombin activity in blood is reduced too much or not enough. It is distressing to note that many patients take dicumarol without adequate laboratory control by determination of prothrombin activity.

Sympathectomy

Some comment should be made on the use of sympathectomy for peripheral vascular disease. Appropriate sympathectomy almost invariably relieves Raynaud's disease of the feet. For reasons wholly unknown to me it fails in at least a third of the cases in which it is performed for Raynaud's disease of the hands. When Raynaud's syndrome is associated with acrosclerosis, sympathectomy is valueless.

As a method of treating essential hypertension, sympathectomy has been almost wholly abandoned. This is because it produces satisfactory results in not more than a third of the instances in which it is used against essential hypertension, and because treatment of this disease with drugs has improved enormously. There are, I believe, only two indications for the use of sympathectomy in the treatment of hypertension: failure of adequate control with drugs, and disinclination on the part of a patient to undertake a program of treatment with drugs which must be carried out indefinitely.

For patients with impaired circulation to the legs, sympathectomy is used somewhat less frequently than it used to be, chiefly because surgical measures are applied directly to the arteries more frequently. In most instances we do not know what the clinical course of arteriosclerosis obliterans will be. Often it is a very benign disease; occasionally it necessitates amputation. People with arteriosclerosis obliterans die from the complications of atheromatosis of the cerebral and coronary arteries more often than from the primary affliction itself. I believe it is true that the major aim of all treatment including sympathectomy is preservation of the extremities until the patient dies of some other condition. Sympathectomy for impaired circulation to the legs is on a sound theoretical basis, for it improves circulation to the skin, in which gangrene ordinarily begins if it occurs. Unfortunately for the desire for complete information, there has been no case-matching to indicate whether or not sympathectomy saves limbs; but I believe it does in many instances.

Sympathectomy is not indicated for the relief of intermittent claudication, which seldom is lessened thereby.

Miscellaneous Conditions

The symptom of claudication is annoying; but owing to the lack of need to walk far, it seldom is accounted disabling. In consideration of this symptom I must say with candor that there is little evidence that any medication influences claudication favorably.

The treatment of sudden arterial occlusion—particularly that resulting from emboli—has been signally improved, although the evidence is not entirely clear that either surgical or nonsurgical treatment has the greater virtue in many instances. The treatment of varices by excision is a forward step of much importance. The use of cortisone or similar steroids has improved remarkably the outlook for patients with polyarteritis and cranial arteritis.

Comment

As I consider again what I have written, I find a substantial amount of pessimism which I had not intended, nor do I intend to close this

(Continued on Page 265)

The Physiologic Action of Ganglionic and Adrenergic Blocking Agents on the Peripheral Circulation

HAROLD D. GREEN, M.D.
Winston-Salem, North Carolina

PERIPHERAL VASCULAR DISEASE affecting the extremities can be divided into two major components: vasospastic and obliterative. Vasospastic vascular disease may be primary or may be associated with obliterative disease inducing symptoms referable only to the skin. It is uncertain, at the present time, whether the vasospasm is due to the hypersensitivity of the terminal arteries, arterioles and precapillary sphincters in association with a normal intensity of sympathetic vasoconstrictor impulses and/or circulating constrictor substances; or whether it is due to a heightened intensity of these impulses or substances. In either case, a basic mode of attack on the vasospastic component is blockade either of the neurogenic pathways or of the receptor areas on the smooth muscle in the walls of the arterioles.

The obliterative component may be due to thickening of the intima often with segmental thrombosis superimposed on an area of intimal damage. The symptoms may be referred to the skin or muscle. At the moment there seems to be no appropriate pharmacologic attack on the obliterative process itself although other papers in this symposium discuss prophylaxis of the atherosclerotic type of obliterative vascular disease. However, it is probable that the development of collateral circulation around any region of segmental occlusion may be hastened by inducing a prolonged demand for blood distal to this area. By this process some long term improvement of even the obliterative vascular disease may be brought about. This can be accomplished in part by maintaining a vasodilation in the terminal arteries and arterioles distal to the occlusion by the use of blocking and vasodilator agents, alone or in combination.

Three categories of drugs are being used at present in inducing vasodilation in patients with vascular disease. These include: (a) the adrenergic blocking drugs, (b) the ganglionic blocking drugs and (c) drugs having a direct vasodilator action on the arterioles. The following is a discussion of the physiologic effects and some of the pharmacologic properties of these agents.

Adrenergic Blocking Drugs

Intra-arterial or intravenous injections of the adrenergic blocking drugs may induce only a brief vasodilation; yet, by observing the effect of the blocking agents on the vasoconstrictor responses induced by adrenergic stimulation, their pharmacologic action can be demonstrated to persist for several hours following their injection.[1,2]

Adrenergic stimulation and blockade in cutaneous vascular beds.—Intra-arterial injections of 0.1 to 1.0 μgm. of arterenol (norepinephrine) or of epinephrine (methyl arterenol) cause vasoconstriction which may reduce the blood flow almost to zero. After two to three minutes, the blood flow gradually returns to the control level without overshoot. Stimulation of the lumbar sympathetic chain induces a similar response. Intra-arterial administration of small doses of one of the adrenergic blocking drugs diminishes the constrictor response to the above forms of adrenergic stimulation. The constrictor response is progressively diminished as the dose of the adrenergic blocking drug is increased. When 3.0 mg/kg of Ilidar® or 0.3 mg/kg of Dibenzyline® is administered, this response is abolished. There is no evidence of any significant reversal, that is, conversion of the constrictor response to a dilator response.[3]

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

From the Departments of Physiology and Pharmacology, and Internal Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, North Carolina.

Much of the data reported in this paper was obtained from studies supported by grants from the Public Health Service (National Heart Institute—Grant H487) and the American Heart Association.

Adrenergic stimulation in skeletal muscle beds.—In man as well as in the dog, intra-arterial injections of minute doses of epinephrine (0.01-0.1 μgm.) cause a slight evanescent vasodilation. Injections of doses as large as 1.0 μgm. may cause a dilation in about 10 per cent of the subjects but in the remainder, a fairly prominent vasoconstriction occurs. In those animals in which 1.0 μgm. induces vasodilation, successive 1.0 μgm. injections convert this to a prominent vasoconstrictor response. Larger doses, that is, 3.0 to 10 μgm., of epinephrine intra-arterially consistently cause a marked vasoconstriction in the skeletal muscle beds of both the dog and man.[4-10] The magnitude of the vasoconstrictor response following intra-arterial injections of all sized doses of arterenol increases linearly with the logarithm of the dose. The constrictor response to epinephrine and often that to the larger doses of arterenol is followed frequently by a phase of vasodilation.[10]

In the dog, stimulation of the lumbar sympathetic chain may produce a fleeting initial dilation but this is usually followed by a prominent constrictor response. Upon cessation of the stimulation a brief phase of dilation may ensue. Administration of atropine abolishes both the initial and terminal dilator responses and after this drug, lumbar sympathetic stimulation produces only vasoconstriction.[10]

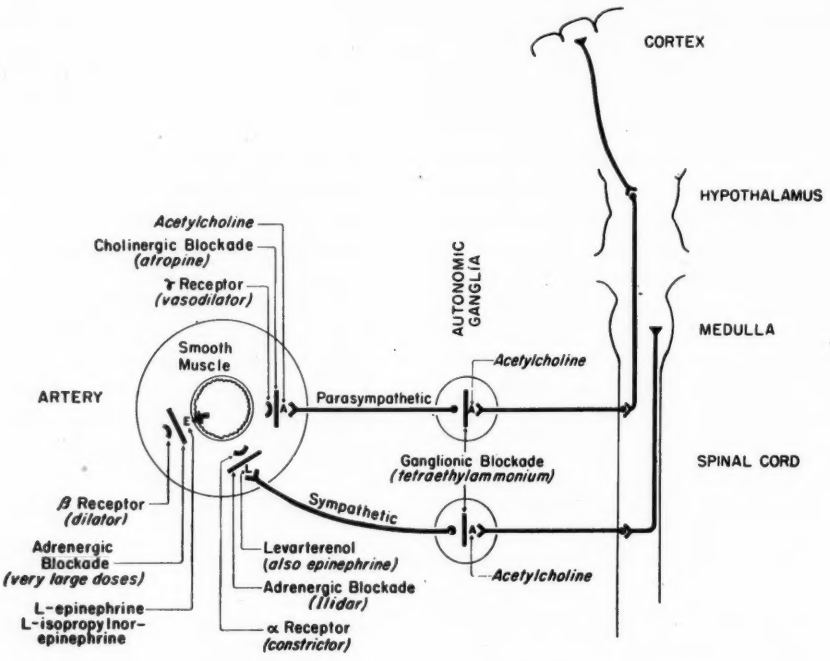


Fig. 1. Schematic diagram of the various receptors in the smooth muscle of the wall of a blood vessel (α, β, γ), of the autonomic ganglionic synapses, and of the sites at which adrenergic and ganglionic blocking drugs act.

Adrenergic blockade in skeletal muscle beds.—Small intra-arterial doses of either of the adrenergic blocking drugs, Ilidar® (0.3 mg/kg) and Dibenzyline® (0.1 mg/kg), diminish the constrictor response to arterenol and that to lumbar sympathetic nerve stimulation, and convert the epinephrine constrictor response to vasodilation. Larger intra-arterial doses of the adrenergic blocking drugs, Ilidar® (30 mg/kg) and Dibenzyline® (3 to 10 mg/kg), abolish the constrictor responses to lumbar sympathetic stimulation and to arterenol. These doses may unmask a slight arterenol dilator response, but only serve to intensify the vasodilator responses to epinephine. Administration of atropine at this time has no effect on the dilator response to epinephrine but abolishes any

vasodilator response to lumbar sympathetic nerve stimulation or to arterenol that may have been unmasked by the adrenergic blocking drug.[10]

Extremely large doses of the adrenergic blocking drugs appear at times to abolish the dilator response to epinephrine.[10] This is a true blockade in the case of Ilidar. However, with dibenzyline this is only apparent and is due to the development of maximal vasodilation which appears to persist for an extremely long time following the injection of epinephrine during the existence of a high degree of adrenergic blockade. Restoration of some degree of vasomotor tone by the intra-arterial injection of pitressin restores the vasodilator capacity as shown by the fact that epinephrine injected following pitressin again induces a vasodilator response.[5]

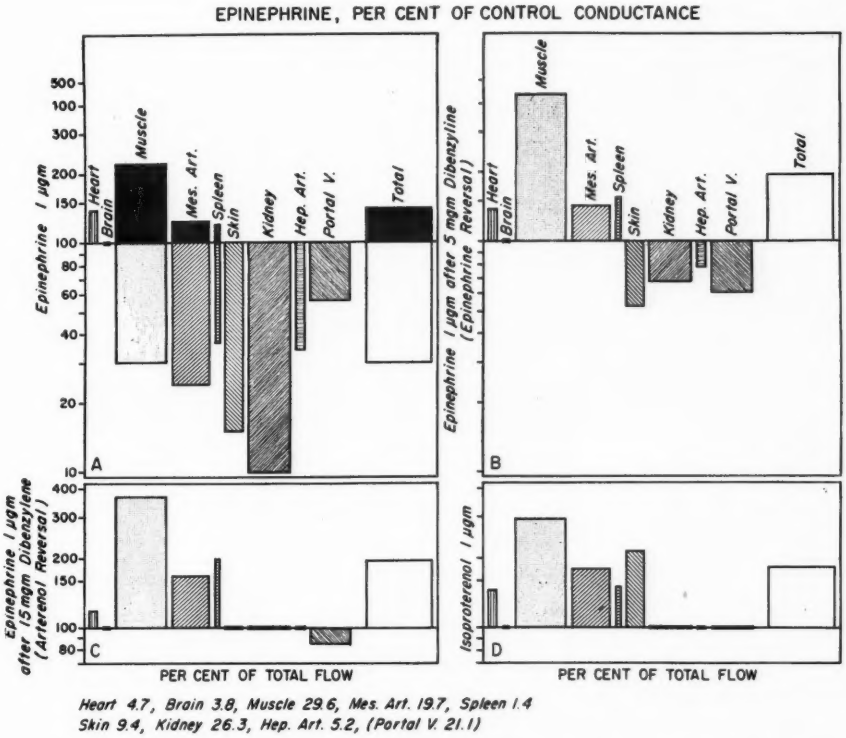


Fig. 2. Response in various vascular beds of the dog to intra-arterial injections of 1 µg. of epinephrine: (A) during a control state, (B) after 5 mg. of Dibenzyline® (or 15 mg. of Ilidar®) intra-arterially, (C) after 15 mg. of Dibenzyline® (or 50 to 100 mg. of Ilidar) intra-arterially, (D) responses to 1 µg. of Isoproterenol (Isopropylnorepinephrine, Isuprel®) intra-arterially during the control state. Ordinate scale indicates response expressed as per cent of control conductance. Conductance = Flow in ml./pressure in mm. Hg.; 100 = no response, greater than 100 = vasodilation, less than 100 = vasoconstrcition. Abscissal scale is drawn approximately proportional to the per cent of the cardiac output flowing in each vascular bed. Total = the calculated change in total body conductance, computed from the sum of the conductance change in each bed, weighted by the per cent of the cardiac output flowing in that bed. Black on white symbols, principally below the 100 line in A, = first or primary response; white on black = secondary response.

Vascular receptors.—From the above studies it can be concluded that in cutaneous vascular beds there are predominantly alpha (constrictor) adrenergic receptors which are stimulated approximately equally by epinephrine, arterenol and through the lumbar sympathetic fibers. These receptors are moderately readily blocked by the adrenergic blocking drugs. In the skeletal muscle vascular bed, alpha adrenergic receptors are also

present and are innervated by the lumbar sympathetic fibers. Also present in the vasculature of skeletal muscle are beta receptors which respond to epinephrine and which can also be shown to respond to isoproterenol (isopropylarterenol). These receptors are not innervated and are highly resistant to blockade by the adrenergic blocking drugs. Such receptors are only minimally present in the vasculature of the skin. In the muscle vascular beds it is obvious that arterenol or an arterenol-like substance rather than epinephrine is the mediator of the sympathetic constrictor impulses since there is no significant reversal of either the arterenol-induced or sympathetic nerve-induced constriction. Also present in skeletal muscle are gamma, or cholinergic, receptors which respond to intra-arterial injections of acetylcholine and which are innervated by autonomic fibers traveling in the lumbar sympathetic chain. These receptors are not affected appreciably by the adrenergic blocking drugs but are readily blocked by atropine.

Extensive studies by Folkow and his collaborators[11] demonstrate that the sympathetically innervated alpha (adrenergic) receptors respond to the medullary homeostatic mechanisms in the regulation of arterial pressure, whereas the sympathetically innervated gamma (cholinergic) receptors do not. On the other hand, the gamma receptors are under the control of the hypothalamus and cortex and probably serve to regulate the blood flow in skeletal muscle in accordance with or in anticipation of skeletal muscle activity. Adjustment of the blood flow to the needs of skeletal muscle does not appear to be mediated by way of the alpha (adrenergic) receptors or by way of the adrenergic mediated autonomic fibers in the lum-

(Turn to Page 245)

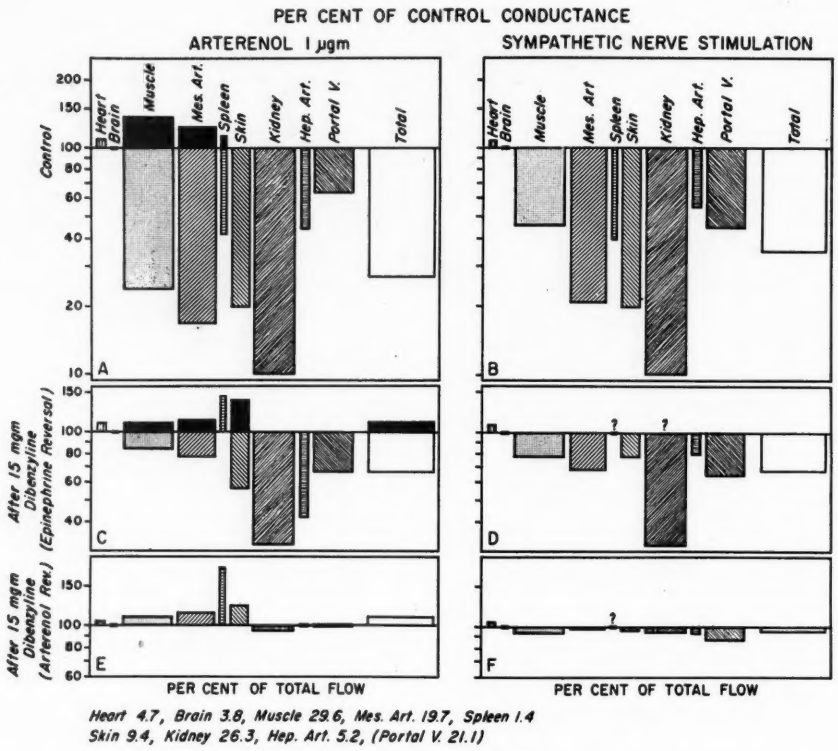


Fig. 3. Responses in various vascular beds of the dog to intra-arterial injections of 1 µg. of 1-arterenol (1-norepinephrine), A, C and E, and to lumbar sympathetic nerve stimulation, B, D and F. A and B in a control state, C and D after 5 mg. of Dibenzyline® intra-arterially and E and F after 15 mg. of Dibenzyline® intra-arterially. Black on white symbols, principally below the 100 per cent line, indicate primary response, and white on black, all of which are above the 100 per cent line, indicate secondary response.

bar chain. The above receptors are illustrated in Figure 1 which also shows schematically the site of action of the adrenergic blocking substances on the alpha receptors and the site of action of the splenic, cutaneous, and renal vascular beds, in the mesenteric and hepatic arteries and in the hepatic portal venous vascular beds (Fig. 2A). Secondary dilation may occur in the skeletal muscle and

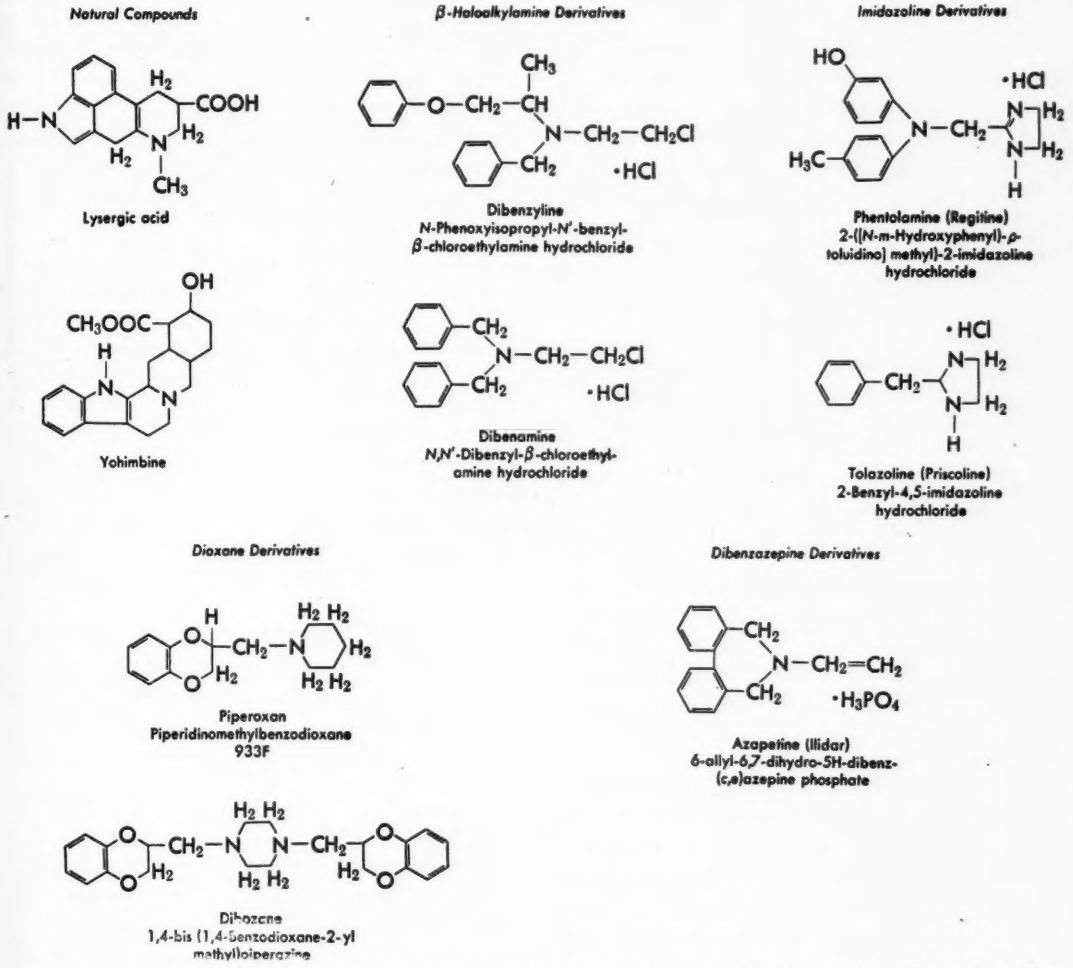


Fig. 4. Structural formulae for various substances which possess adrenergic blocking action (Reproduced from Drill, Pharmacology in Medicine[17]).

cholinergic blocking agents on the gamma receptors.

Effects of Adrenergic Blockade and Adrenergic Stimulation on Other Vascular Beds.—In order to appreciate the potential usefulness of the adrenergic and ganglionic blocking drugs, it is desirable to know what the effects of adrenergic stimulation and blockade would be in the other major vascular beds in the body. Epinephrine causes primary vasoconstriction in skeletal muscle, in the mesenteric arterial beds. No response occurs in the cerebral bed; and in the coronary bed a mild vasodilation may be elicited. During adrenergic blockade, the constrictor responses are progressively reduced and, in the case of skeletal muscle, mesenteric artery and splenic beds, the constrictor responses are reversed, that is, converted to vasodilator responses (Fig. 2B). Because of the overall magnitude of the flow in these beds as compared with that in the other beds, the net effect on the total vascular resistance in the body after ap-

propriate doses of the adrenergic blocking drugs given intravenously is vasodilation. Arterenol and sympathetic nerve stimulation cause vasoconstriction in the various vascular beds in a manner exactly comparable to that of epinephrine (Fig. 3). Reversal of the response to arterenol by Dibenzyline occurs only to a small extent in skeletal muscle, the mesenteric arterial bed, and in the vascular beds of the skin and spleen. Reversal of the adrenergic constrictor response to sympathetic nerve stimulation does not occur.

In view of the above it would appear that moderate doses of the adrenergic blocking drugs might be expected to reduce excessive vasospasm where it exists without causing excessive fall of arterial pressure unless there is an abnormal quantity of epinephrine circulating in the body. If such is present, however, the marked vasodilator responses which would occur in the two large vascular beds, skeletal muscle and the mesenteric bed, might be expected to decrease the total peripheral resistance producing a significant fall in the arterial pressure impairing the cerebral, coronary and renal circulations, in which reversal does not occur.

Available Preparations.—The adrenergic blocking drugs which are available at the present time are indicated in Figure 4. For oral administration, the following preparations are available: azapetine (Ilidar®) 25 mg. tablets, phenoxybenzamine (Dibenzyline®) 10 mg. capsules, and tolazoline (Priscoline®) 25 mg. tablets. A common factor in all of these is a tertiary nitrogen, usually linked directly or through a single carbon atom with one or two benzine rings. The nitrogen may be linked also with an imidazoline ring or with a two-carbon aliphatic chain containing chlorine such as is seen in Dibenzyline,® or an unsaturated linkage such as is seen in Ilidar.

Evaluation of the Effects of These Drugs in Man.—In man, the blocking effects of these drugs have been studied by recording the cutaneous blood flow determined with the thermocouple, measuring the skin temperature on the tips of the toes and fingers while the subjects are exposed in the constant temperature room in which the air is circulating relatively rapidly (25-50 feet/min. at an ambient temperature of 20°C). This technique is the equivalent of the calorimetric method of measuring blood flow and the rate of circulation can be approximated closely by determining the temperature of the skin when it comes into equilibrium. When the skin temperature approximates the room temperature, the blood flow is extremely low. As the skin temperature approximates body temperature, the blood flow must increase as much as 100-fold over that when the skin temperature is at its minimal point. A minimum rate of blood flow, that is, maximal vasoconstriction, may be induced by exposing subjects to this environmental temperature while they are clad only in shorts or a slip for from a half to one and one-half hours, provided they have not eaten or exercised during the hour or two prior to the exposure.

The ability of the adrenergic blocking drugs to block this neurogenically induced vasoconstriction can be studied by slowly administering the drugs intravenously over the course of a half hour while maintaining the exposure to the cool environment. Figure 5 shows the results of such studies on ten medical students. The doses of the adrenergic blocking drugs were the maximal doses which the student could tolerate without untoward symptoms during the study and without the occurrence of excessive postural hypotension following the study. On the basis of this choice of doses, Ilidar® was the most effective; Priscoline® and Regitine® less effective, respectively; and Dibenzyline® almost ineffective except in the upper extremities. Consistently in studies such as this, the vasodilator response has been more marked in the upper than in the lower extremities.[12,13]

Clinical Use of the Drugs.—The adrenergic blocking drugs may be given intra-arterially in acute emergencies though it is perhaps safer to administer them by intravenous drip. For prolonged administration it is more satisfactory to give the drugs orally. In oral administration one tablet four times a day is prescribed initially and every two to three days the dose is increased by one tablet until the maximum tolerated dose is reached. In the case of Ilidar this is usually three to four tablets four times a day.

The principal side effects which may be noted with these drugs are those due to postural hypotension which may ensue when the maximum dosage is used. The symptoms include dizziness, nausea and fainting. Such hypotension is rarely severe, but should be avoided in patients with atherosclerosis. This difficulty has been more prominent with Dibenzyline® than with the other drugs due, perhaps, in part to the more prolonged

action of this substance and its greater tendency to cause epinephrine reversal. Tachycardia and palpitation have been reported by many investigators but when the patient gradually adjusts the dose, palpitation has not been a prominent symptom. In case a patient develops an intercurrent infection, particularly a viral infection, it is well to reduce the dose or discontinue the use of these drugs until full recovery from the infection has occurred, since the infection tends to potentiate the postural hypotension induced by the drugs. Cutis anserina, that is, gooseflesh, formication and chilliness are prominent with Priscoline® but do not occur with the other drugs. All these drugs may occasionally produce gastrointestinal disturbances. About 2 per cent of the patients taking Ilidar® will experience a drug fever, characterized by flu-like symptoms of aching, chills and fever amounting to 101-103°F. These symptoms subside within eight to twenty-four hours after discontinuing the drug. This drug fever does not usually occur until after two or more weeks of continuous administration. Should such symptoms develop, the patient should be shifted to another drug since the sensitivity appears to persist indefinitely.[14]

In our hands, improvement of vasospastic symptoms and, with prolonged use, some improvement of the walking distance due to development of collateral circulation, has been obtained in a large proportion of patients.[14,15] A small number of patients in whom the vasospasm is so severe that it cannot be overcome without the occurrence of severe side effects may require sympathectomy. We have not seen any immediate relief of the symptom of intermittent claudication with the use of any of these drugs. This is of interest since, because of the phenomenon of epinephrine reversal, one might anticipate a more marked vasodilator effect in skeletal muscle than in skin. However, it is probable that the vasodilator response to ischemia in skeletal muscle produces a maximal vasodilator effect which cannot be enhanced by blockade of the sympathetic fibers or of circulating adrenergic substances.

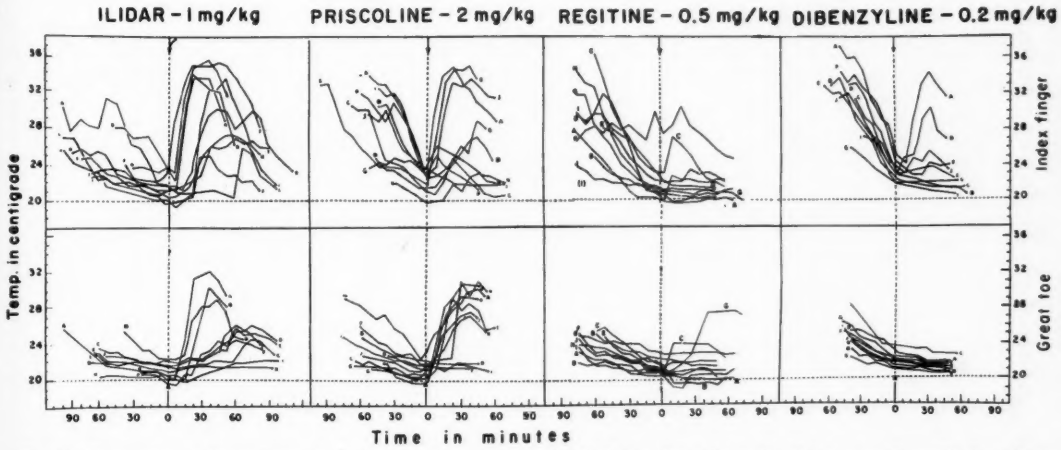


Fig. 5. Responses to intravenous infusions of four adrenergic blocking drugs in each of ten normal medical students. Ordinate scale indicates skin temperature of an index finger (upper curves); and the large toe (lower curves) expressed in degress Centigrade. Room temperature 20°C., range ± 0.3°C., air velocity 50 feet per second. Throughout the study the subjects were fasted, and were exposed, clad only in shorts. Temperatures close to room temperature indicate maximal vasoconstriction; temperatures close to 36°C., maximal vasodilation. (Reproduced in modified form from references 12 and 13).

Ganglionic Blockade

Unlike the adrenergic blocking drugs, intra-arterial injections of the ganglionic blocking drugs have no vasodilator effect on the terminal arteries, arterioles or precapillary sphincters. In fact, a slight vasoconstriction may be induced by the intra-arterial injections. These substances do not have any effect on the responses to the intra-arterial injections of the adrenergic substances, nor on the responses to postganglionic stimulation of the sympathetic fibers. The ganglionic blocking drugs do, however, block transmission at the ganglion of both the sympathetic (adrenergic) and the parasympathetic (cholinergic) autonomic impulses. Presumably these ganglionic blocking

agents also block the release of adrenalin from the adrenal gland in response to splanchnic nerve stimulation. The site of action of the ganglionic blocking drugs is portrayed in Figures 1 and 6.

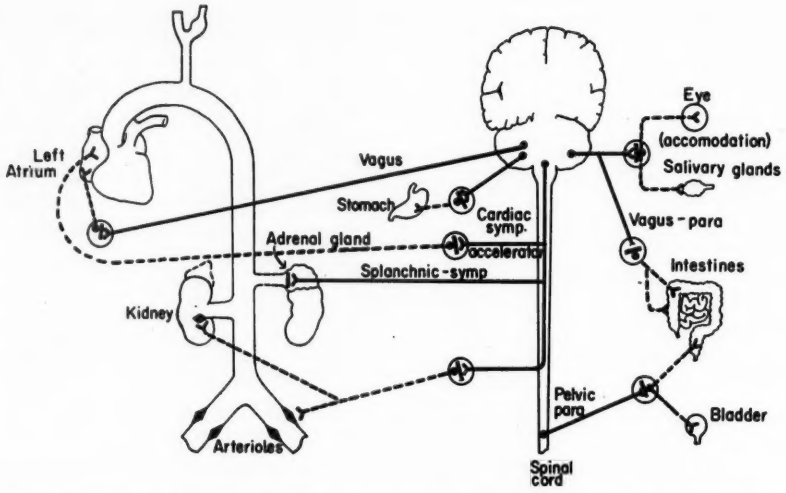


Fig. 6. Ganglionic blockade. Diagram of the sites of action of the ganglionic blocking drugs on the sympathetic (left side exclusive of the vagus) and parasympathetic (right side) divisions of the autonomic nervous system. Dashed lines indicate the fibers in which the number of impulses is reduced as a result of the blockade, solid line indicates neuronal activity which is blocked and heavy solid bar indicates blockade. (Reproduced from reference 18). Blockade of the vagus to the heart would lead to speeding of the heart, but this is counterbalanced by blockade of the sympathetic fibers which would lead to cardiac slowing. See text for further discussion.

Available Preparations.—The various preparations which have been used experimentally in the past and which are now available for clinical use are shown in Figure 7. All of these are effective by the parenteral route. By the oral route Ansolysen,® Inversine® and Ecolid® are quite effective, hexamethonium is slightly effective, and the others are without significant effect. For oral administration the following are available: hexamethonium 125 and 250 mg. tablets; pentolinium (Ansolysen®) 20, 40 and 100 mg. tablets; mecamylamine (Inversine®) 2.5 and 10 mg. tablets and chlorisondamine (Ecolid®) 25 mg. tablets.

Physiologic Studies in Man.—The relative effectiveness of the ganglionic blocking drugs in man can be studied by the same technique as that described above for the adrenergic blocking drugs. The responses to some doses which appeared to be reasonably safe are illustrated in Figure 8. Etamon,® Arfonad® and hexamethonium appear to be the most consistently effective of these particular agents. In contrast to the adrenergic blocking drugs, the ganglionic blocking drugs appear to be more effective on the lower extremities. No satisfactory explanation for the difference in the effectiveness of the adrenergic and ganglionic blocking drugs on the upper and lower extremities exists. Since the ganglionic blocking drugs can exert an effect only on neurogenic tone, it is possible that the difference in the responses to the two groups of blocking drugs may be interpreted as indicating that neurogenic control of vasoconstriction is more prominent in the lower than in the upper extremities. Conversely, it is possible that circulating adrenergic constrictor substances are relatively more important in the upper extremities. If this is the case, it might offer one explanation for the clinical observation that sympathectomy is often more effective in relieving vasospasm in the lower than in the upper extremities.

Side Effects.—The side effects of the ganglionic blocking drugs are those which might be expected from blockade of both the sympathetic and parasympathetic portions of the autonomic nervous system. Those due to sympathetic blockade are primarily postural hypotension, as manifested by

weakness, dizziness and fainting. This may be experienced particularly when arising suddenly from a lying or sitting position. Hypotensive reactions may occur more readily with the ganglionic than vision and obstipation as the principal undesirable effects. The blurring of near vision is more prominent in patients approaching the presbyopic age and may necessitate the use of stronger reading

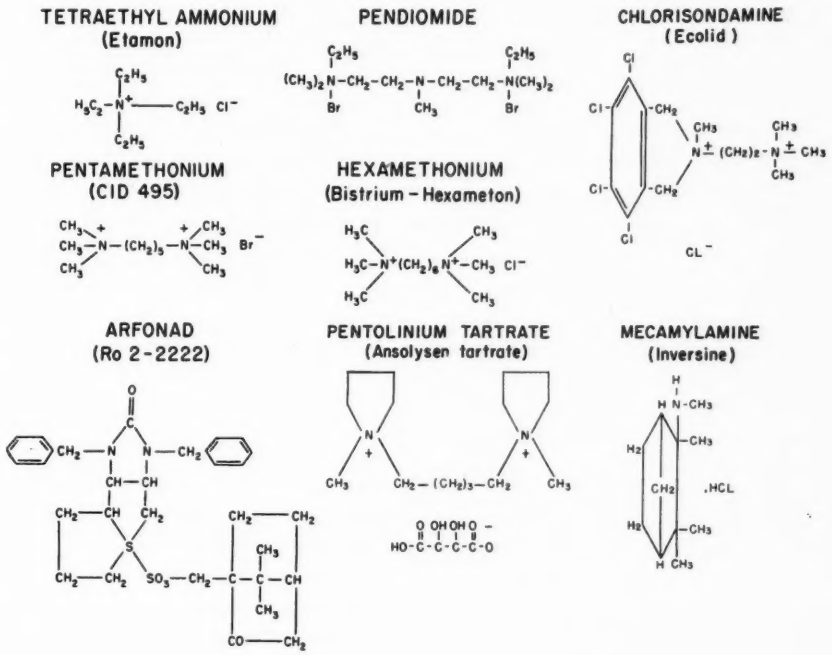


Fig. 7. Structural formulae for a number of ganglionic blocking drugs which have been used either experimentally or clinically.

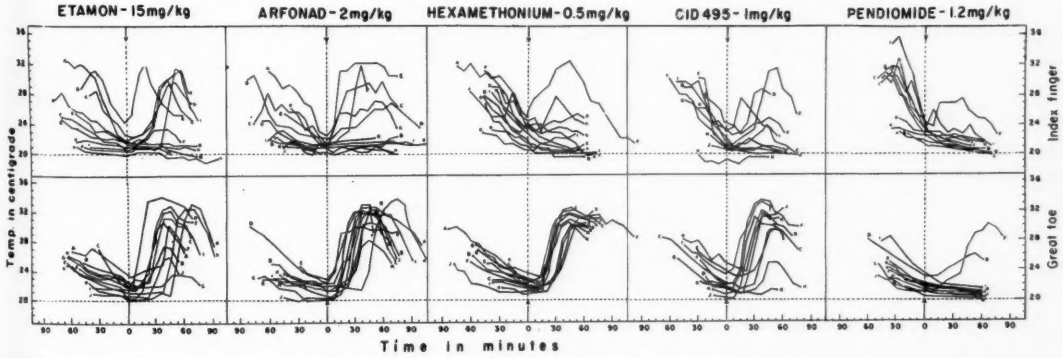


Fig. 8. Responses in ten normal medical students to each of five ganglionic blocking drugs. See legend to Figure 5 for details.

with the adrenergic blocking drugs. Such reactions should be avoided in atherosclerotic patients since they may induce cerebral or myocardial infarction. Blockade of the parasympathetic system leads to dryness of the mouth, blurring of near glasses. Obstipation is a significant problem and appears to be alleviated most readily by the use of approximately 15 mg. of Prostigmine in the morning and if necessary the additional use of cascara, 4 to 8 cc. at bedtime. If the patient fails

to have a bowel movement, further use of the blocking drug should be suspended until elimination is re-established.[16]

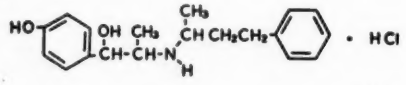


Fig. 9. Structural formula for nylidrin hydrochloride (Arlidin®).

Direct Acting Vasodilators

Nylidin hydrochloride (Arlidin®) is a substance classified in the New and Non-Official Remedies as an adrenergic substance. Part of its structural formula is similar to epinephrine (Fig. 9). This substance is stated to cause vasodilation in muscle but to have no vasodilator effects in cutaneous beds. It was originally promoted for its supposed ability to relieve intermittent claudication by virtue of its muscle vasodilator effects. In our hands, this drug causes vasodilation in the dog in both muscle and cutaneous vascular beds and when given by intravenous drip to human subjects (as in the above studies) causes a prominent vasodilation in the fingers and a weak vasodilation in the toes.

When given to patients by mouth, this substance causes cutaneous vasodilation. In our hands, however, it has no immediate effect on the symptom of intermittent claudication. As with the adrenergic blocking drugs, prolonged use of Arlidin® may stimulate collateral circulation development.

The mechanism of the Arlidin® vasodilation is not established. It is possible that it effects beta receptors in a manner similar to isoproterenol. The effects of adrenergic blockade on this substance are not known. Clinically, it has proven possible to give the drug along with adrenergic blocking drugs with apparently some synergistic effect and without accentuating the hypotensive effects of either drug (work in preparation).

The drug can be administered initially in doses of 6 mg. four times a day and in many patients this can be increased progressively to 18 to 24 mg. four times a day. Postural hypotension does not seem to be a prominent side effect, but patients may complain of considerable nervousness following doses of 12 to 18 mg. When this occurs, the dose should be held at this level or reduced rather than increased. Another similar drug which is undergoing evaluation is Duvadilan.®

Alcohol.—Ethyl alcohol in a dose of 60 to 120 ml. of 100-proof whisky given orally causes a marked cutaneous vasodilator effect in normal human subjects demonstrated by using the above technique of study. This vasodilation is obtained consistently in both upper and lower extremities though it occurs more quickly and completely in the upper extremities. The exact mechanism of the alcohol dilator effect is not known.

Diagnostic and Clinical Usefulness of the Above Drugs

In normal subjects, administration of any of the above drugs in adequate dosage simultaneously with warming of the torso with blankets plus two 30 watt electric heating pads completely relaxes the vasospasm induced in both upper and lower extremities by the exposure to a cool environment. Use of one of these drugs together with body warming therefore provides an effective and convenient means for differentiating vasospasm from obliterative disease affecting the cutaneous circulation in patients. This technique also gives a method for evaluating the severity of obliterative disease, and, by successive studies at weekly to monthly intervals, allows one to evaluate the development of collateral circulation to the skin. Studies of this type are also quite useful in evaluating the effectiveness of sympathectomy. In most cases, postsympathectomy studies yield skin temperatures within 1 to 2° of those predicted during the presympathectomy study (Fig. 10).

Summary and Conclusions

From the above studies it appears that the vasospastic component of peripheral vascular disease may be attacked: (a) by establishing a blockade at the alpha constrictor receptor endings of the terminal arteries, arterioles and precapillary sphincters, by the use of the adrenergic blocking drugs; (b) by relief of the neurogenic component of vasospasm by blocking the sympathetic constrictor impulses at the ganglia by the use of the ganglionic blocking drugs; and (c) by direct induction of vasodilation by the use of substances such as alcohol and Arlidin.® One, or a combination of these drugs may serve effectively in the relief of vasospasm and in stimulating the development of collateral circulation thus providing a medical approach to the control of vascular disease which in many cases is comparable to that obtainable by sympathectomy. Even after sym-

pathectomy some additional benefit may occasionally be obtained by the administration of one of the above drugs.

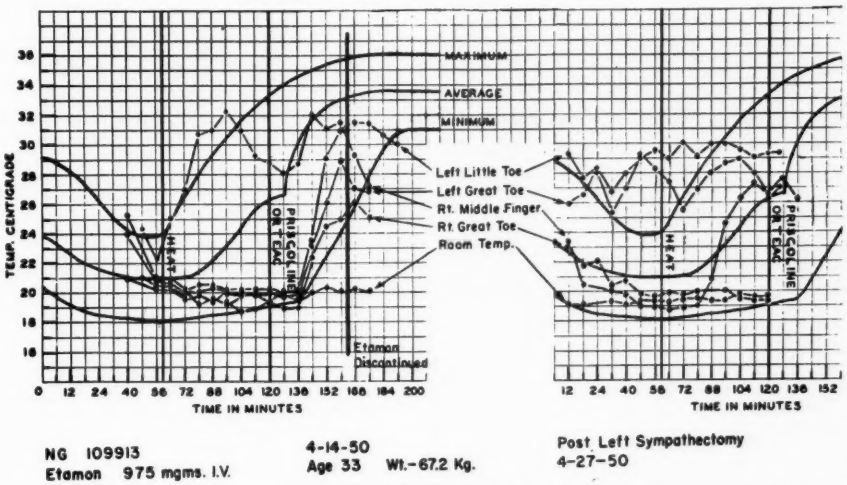


Fig. 10. Skin temperature responses to body warming plus an intravenous infusion of Etamon® in a patient with "vascular disease," prior to sympathectomy—left side. Skin temperatures recorded without the drug in the same patient after a left lumbar sympathectomy. Note that the left toe temperatures stabilized at approximately the same level following the sympathectomy as that obtained in the presympathectomy study.

The principal side effects of these drugs include: (a) postural hypotension, seen with both the adrenergic and the ganglionic blocking drugs; (b) symptoms referrable to the skin, that is, chilliness, cutis anserina and formication, seen with Priscoline;® (c) drug fever seen with Ilidar,® and (d) excessive nervousness seen with Arlidin.®

Appropriate use of these drugs provides: (a) a means for evaluating the degree of vasospasm, and for predicting the probable benefit of drug administration or sympathectomy; (b) with prolonged usage, amelioration of many of the symptoms due to the vasospastic component of peripheral vascular disease; and (c) for development of collateral circulation which may be of assistance in the relief of the obliterative component of the disease.

References

1. Roberts, Gwen, Richardson, A. W. and Green, H. D.: Effects of Regitine (C-7337) upon the blood flow responses to epinephrine in the innervated hind limb of the dog. J. Pharmacol. & Exp. Therap., 105:466, 1952.
2. Moore, P. E., Richardson, A. W. and Green, H. D.: Effects of a new dibenzazepine derivative, Ro 2-3248, 6-allyl-6, 7-dihydro-5H-dibenz [c, e] azepine phosphate, upon the blood flow, the peripheral resistance and the response to injections of epinephrine of the innervated hind limb of the dog. J. Pharmacol. & Exp. Therap., 106:14, 1952.
3. Green, H. D., McLeod, J. A., Anderson, D. A. and Denison, A. B., Jr.: Comparison of the blockade produced by Dibenzyline, Ilidar, Tolazoline and Phentolamine of the vasomotor responses in skin induced by sympathetic nerve stimulation with the blockade of its responses to 1-epinephrine and 1-norepinephrine. J. Pharmacol. & Exp. Therap., 112:218, 1954.
4. Lanier, J. T., Green, H. D., Hardaway, J., Johnson, H. D. and Donald, W. D.: Fundamental difference in the reactivity of the blood vessels in skin compared with those in muscle. Blood flow response in these two beds to ischemia and to intra-arterial injections of methacholine, epinephrine and noradrenalin before and after administration of antiadrenergic drugs. Circulation Res., 1:40, 1953.
5. Rapela, C. E., Orovitz, N. F. and Green, H. D.: Vasomotor tone and epinephrine reversal. Fall Physiology Meeting, Chicago, 1957.
6. Bock, K. D., Hensel, H. and Ruef, J.: Die Wirkung von Adrenalin und Noradrenalin auf die Muskel- und Hautdurchblutung des Menchen. Pflügers Arch. ges. Physiol., 261:322, 1955.
7. Bell, D. M. and Stead E. A., Jr.: Effects of epinephrine on the vessels of the calf. Observations on the period of initial vasodilation. J. Appl. Physiol., 5:228, 1952.
8. Duff, R. S. and Swan, H. J. C.: Further observations on the effect of adrenaline on the blood flow through human skeletal muscle. J. Physiol., 114:41, 1951.
9. Allen, W. J., Barcroft, H. and Edholm, O. G.: On the action of adrenalin on blood vessels in human skeletal muscle. J. Physiol., 105:255, 1946.
10. Youmans, P. L., Green, H. D. and Denison, A. B., Jr.: Nature of the vasodilator and vasoconstrictor receptors in skeletal muscle of the dog. Circulation Res., 3:171, 1955.

(Continued on Page 272)

Fundamentals of Anticoagulant Therapy

NELSON W. BARKER, M.D.
Rochester, Minnesota

ANTICOAGULANT THERAPY has been employed to prevent intravascular thrombosis for almost twenty years. During the past ten years, its use has been gradually extended on the basis of cumulative experience. Most anticoagulant therapy now is carried out by the employment of one of the coumarin compounds, but in certain situations, heparin is still a valuable anticoagulant and one for which there is currently no available satisfactory substitute.

Heparin

The advantage of heparin is that it produces a therapeutic anticoagulant effect within a few minutes and this effect can be terminated rapidly by stopping administration of the drug, or even more rapidly by the intravenous injection of protamine sulfate. The disadvantages of heparin are that it is costly and it must be administered parenterally. Thus, heparin is not a satisfactory anticoagulant for therapy longer in duration than a few days or weeks. Currently, heparin is used mostly to cover the period between initiation of treatment and achievement of the therapeutic effect of the coumarin compounds, which act more slowly. Administration of both heparin and a coumarin compound is started simultaneously, and the use of heparin is discontinued as soon as tests show that the coumarin effect is established. Short-term anticoagulant therapy occasionally is maintained for a few weeks by use of heparin alone, when for some reason it is inadvisable to employ one of the coumarin compounds.

The degree of anticoagulant effect of fixed doses of heparin varies as greatly among different patients as does that of fixed doses of one of the coumarin compounds. Therefore, regardless of the method by which heparin is administered, it is desirable to check the effect by determination of the coagulation time of whole blood in order to establish the optimal dose and frequency of administration of heparin for each individual patient. However, this is not always practical. When treatment is only given for a few days, fixed dosage schedules for heparin often are employed without determining the degree of its effect.

In my experience, a satisfactory response to heparin for short-term therapy usually is achieved in most patients by the intermittent intravenous injection of 50 mg. every four hours. Less satisfactory effects are obtained by the deep subcutaneous injection of 100 to 200 mg. in a concentrated aqueous solution every twelve hours. This involves considerably fewer injections but introduces the variable of the rate of absorption and increases the variability of effect among different patients, so that more of them will have insufficient anticoagulant effect for certain periods of the day and therefore be unprotected against the condition for which the drug is given. Also, a few will have an excessive effect that may be sufficient to cause serious bleeding. The most satisfactory method of giving heparin in order to achieve the exact degree of anticoagulant effect desired for the individual patient is by the continuous intravenous injection of a dilute solution. The rate of administration is then guided by the coagulation time of whole blood in an effort to maintain the coagulation time between fifteen and twenty-five minutes, or approximately two to four times the normal. This method requires close supervision and much expenditure of time for each patient and is, therefore, not practical in many situations.

Heparin is a powerful anticoagulant drug. The therapeutic effect of adequate doses of heparin is considerably more profound as far as disturbance of the coagulation mechanism is concerned than is that of the coumarin compounds; the danger of hemorrhage is greater with therapeutic doses of heparin than it is with therapeutic doses of the coumarin compounds. When bleeding occurs dur-

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

Dr. Barker is Professor of Medicine at the Mayo Foundation. The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

ing the administration of heparin and if it is recognized quickly, it can be terminated more rapidly because the action of heparin can be halted more rapidly, but if the bleeding is internal and therefore not easily recognized, a dangerous situation may develop before the effect of heparin is terminated.

Untoward reactions to heparin other than the possibility of bleeding are few and consist of allergic or anaphylactic phenomena. All such reactions reported to date have occurred among patients who have had allergies to other agents, particularly among those with allergic asthma. Therefore, in any patient who has a history of allergic asthma, cutaneous tests for sensitivity to heparin should be done before large doses of the drug are administered.

Heparin prolongs the prothrombin time as determined by the one-stage technique. When heparin is given to cover the first twenty-four or forty-eight hours of anticoagulant therapy and administration of one of the coumarin compounds is started at the same time, the most satisfactory method of giving the heparin is by intermittent intravenous injections every four hours. A test of the prothrombin time to determine whether the effect of the coumarin compound has reached the therapeutic range should be done only on a sample of blood drawn at least four hours after a dose of heparin has been given, because otherwise the prothrombin time will reflect the combined effect of the coumarin compound and heparin.

Coumarin Compounds

Bishydroxycoumarin (dicumarol) is still the most widely used of the coumarin compounds for anticoagulant effect. Ethyl biscoumacetate (tromexan) has a somewhat more rapid action that terminates somewhat more rapidly when its use is discontinued, but many physicians consider that the effect of tromexan is more erratic, particularly during the first few weeks of administration. When dicumarol is used, the addition of a single dose of 900 to 1,200 mg. of tromexan to the original 300-mg. induction dose of dicumarol will produce a more rapid anticoagulant effect; the prothrombin time will be brought into the therapeutic range within twenty-four hours in about 40 per cent of patients and within forty-eight hours in an additional 50 per cent. With this combination, effects exceeding the therapeutic range will develop within the first few days in approximately 20 per cent of patients.

A recent addition to the coumarin compounds available for therapeutic use is warfarin (coumadin) sodium. Warfarin sodium is soluble in water to a far greater extent than are any of the other coumarin compounds or phenindione. It is the only one that may be given intravenously or intramuscularly. It has the theoretic advantage of being absorbed completely from the gastrointestinal tract, thus eliminating one factor of variability of response among different patients. However, as with dicumarol, the effects of warfarin sodium are still variable enough among different patients so that no program of fixed doses can be used, and the optimal dose for each patient must be guided by determining prothrombin times. Some physicians consider that a somewhat more rapid and less variable effect can be obtained with warfarin sodium than with dicumarol. Despite conflicting reports, it is doubtful that any one of the coumarin compounds is superior to any other one or that the average physician can employ a particular one with greater ease and still achieve a satisfactory anticoagulant effect. Such effects can be achieved with several agents, and the choice should be left to the individual physician, depending somewhat on his experience and the consistency of his results. If a therapeutic hypoprothrombinemia is established and maintained with any one of these compounds, the patient receives the same protection against thrombosis and encounters the same risk of bleeding.

It must be re-emphasized that different patients vary considerably in their response to coumarin compounds and that any individual patient may vary from time to time in his response to certain fixed doses. Therefore, constant supervision and development of the optimal dose of the compound for each patient are imperative, and this optimal dose can be determined only by trial and error. Daily measurement of the one-stage prothrombin time should be done during the first two or three weeks of treatment at least. If the patient is maintaining a satisfactory response at the end of that time on a fixed daily dose, the frequency of the tests may be gradually decreased to twice or once a week, or even in some instances to once in four weeks. However, the physician must assume the responsibility for doing the test frequently enough to be sure that he is obtaining the proper effect for the individual patient.

Phenindione is not a coumarin compound but it has a similar action and has been recommended by some physicians. Its action resembles that of tromexan in that its effect develops relatively rapidly and disappears rapidly when its administration is discontinued. However, it is more difficult to keep the prothrombin time within the therapeutic range during administration of phenindione than it is with dicumarol or even tromexan.

Long-Term Therapy

For long-term anticoagulant therapy, it has been said that three things are required, namely (1) a co-operative patient, (2) an interested physician and (3) a good laboratory. Physicians who have had long experience in the use of coumarin compounds agree that the one-stage test of prothrombin time is the only satisfactory guide to dosage. I would like to warn against the use of the coagulation time of whole blood for this purpose, although this procedure has been advocated by some investigators. The coagulation time of whole blood is susceptible to numerous errors of technique that cause significant variations in the results. Furthermore, if one depends on this test (even when done by an expert who supposedly has solved all the problems of technique and has done many tests), the anticoagulant effect probably will be excessive in many patients and will result in a considerably increased tendency to bleeding.

In general, a satisfactory therapeutic range of hypoprothrombinemia produced by one of the coumarin compounds is reflected by prothrombin times that are between two and two and one-half times the normal value in seconds for that particular laboratory. These are narrow limits and actually a broader therapeutic zone might be considered as prothrombin times between one and one-half and three times normal, although the narrower range is more desirable, if it is possible to maintain it. However, in discussing the therapeutic range of hypoprothrombinemia, it is best to consider the results of the prothrombin-time test expressed as the degree of prothrombin activity. Normal values for prothrombin time in seconds vary considerably among different laboratories, depending on the exact technique used and particularly on the type of thromboplastin, which is the chief reagent. Many laboratories express results in terms of percentages of prothrombin activity. These should be calculated by interpolation on a dilution curve obtained by plotting the prothrombin times of various dilutions of normal plasma against the percentages of the dilutions. By this method, my colleagues and I consider that the therapeutic range of hypoprothrombinemia for the coumarin compounds is indicated by a prothrombin activity between 10 and 30 per cent. The ideal range is between 15 and 25 per cent.

For long-term coumarin therapy, it is advisable as soon as possible to establish the optimal daily dose for each patient, namely the dose that will maintain the prothrombin time within the therapeutic range. For dicumarol, this dose usually varies between 25 and 125 mg. a day. Sometimes it is necessary to give different doses on alternate days or to give a slightly larger or smaller dose every third or fourth day. Such fine adjustments often are necessary in order to maintain a smooth effect that varies little from day to day as measured by the prothrombin time. Maintenance doses for tromexan usually vary between 300 and 900 mg. a day, and those for warfarin sodium are between 2.5 and 10 mg. a day. The first, or induction, dose of tromexan is 1,200 to 1,500 mg., whereas that of warfarin sodium is 40 to 50 mg.

If the prothrombin time is kept within the therapeutic range, experience has shown that the patient receives maximal protection against thrombosis with minimal danger of hemorrhage. However, an occasional patient may be encountered in whom the stimulus to thrombosis is great and in whom maintenance of the prothrombin time within the therapeutic range is not sufficient to prevent thrombosis. Fortunately, such patients are rare. Also, few patients will experience serious bleeding when the prothrombin time is within the therapeutic range. When such bleeding occurs, it is usually from granulating wounds, ulcers or tumors in the gastrointestinal or urinary tract, or at the site of a contusion or laceration. In most instances of severe bleeding, it will be found that the prothrombin time has been prolonged beyond the therapeutic range. The prothrombin time often may exceed the therapeutic range during the first week of treatment, when the dosage of the drug employed is still in the trial stage. However, in my experience, it is unusual for serious hemorrhage to develop during this first week of treatment, even though the prothrombin time may increase considerably above the therapeutic range, whereas a great deal more danger of hemorrhage exists with such increased prothrombin times during later periods of treatment.

Contraindications

Contraindications to anticoagulant therapy with either heparin or the coumarin compounds are still considered to include blood dyscrasias with a tendency to bleeding, purpura of any type, and recent operations on the brain or spinal cord. In addition, moderate to severe degrees of hepatic or renal insufficiency contraindicate use of the coumarin compounds and phenindione. More than the usual degree of caution must be observed when anticoagulants are given to patients who have ulcerating lesions or granulating wounds and to those who have tubes in various body orifices. Caution should be observed and smaller induction and maintenance doses should be given to patients who have impaired states of nutrition. These include patients who have had surgical operations within the previous five days, those who have been on restricted diets, and those who have gastrointestinal disease, particularly associated with vomiting and diarrhea. Such patients are more than normally sensitive to the coumarin compounds and usually exhibit an excessive response to the doses recommended for patients without nutritional disturbances.

Neutralization of Anticoagulant Effects

For correction of the anticoagulant effect of the coumarin compounds, vitamin K_1 is much more effective than are the water-soluble preparations of menadione. When prothrombin times increase excessively after administration of the usual induction doses of one of the coumarin compounds, this condition may be corrected satisfactorily and the prothrombin time brought back into the therapeutic range by the intravenous administration of menadione sodium bisulfite in a dose of approximately 36 mg. However, when it is necessary to stop the effect of the coumarin compound as rapidly as possible, particularly if serious bleeding has been encountered, it is advisable to use vitamin K_1. This can be given orally and the recommended dose is 250 mg. If the patient is vomiting or has external biliary drainage, it may be given intravenously in the same amount; it is advisable to dilute the material in 300 to 500 ml. of fluid when giving it intravenously. To date there is no evidence that stopping the effect of coumarin compounds by use of these large doses of vitamin K_1 produces hypercoagulability of the blood or a greater tendency to thrombosis than existed prior to administration of the anticoagulant. The large dose of vitamin K_1 is recommended because it will be effective in some cases in which smaller doses, such as 50 mg., will not. Transfusions of whole blood may be advisable when a considerable amount of blood has been lost. In these instances, the transfusions are given to replace blood rather than to replace prothrombin.

Comment

In considering the indications for anticoagulant therapy, the best basic approach is to think of each patient as an individual problem. The likelihood and seriousness of further thrombosis or embolism should be weighed against the difficulty in maintaining and satisfactorily controlling treatment and the possibility of bleeding. In general, short-term anticoagulant therapy is indicated when sural, femoral or iliofemoral thrombophlebitis or pulmonary embolism occurs after surgical operations, childbirth or severe injury, or during the course of infectious diseases. Treatment should be continued for at least two weeks and until the patient has been ambulatory for several days. Similar short-term therapy also is indicated for acute peripheral embolic or thrombotic arterial occlusion. Use of anticoagulants for four to six weeks is indicated in most cases of acute myocardial infarction.

If it can be maintained satisfactorily, long-term anticoagulant therapy usually is indicated in the following conditions: (1) frequently recurring idiopathic thrombophlebitis; (2) chronic auricular fibrillation complicated by intracardiac thrombosis and peripheral or cerebral arterial embolization; (3) recurrent episodes of basilar or carotid insufficiency or cerebral infarcts resulting from thrombosis in the basilar or carotid arterial systems unless such infarcts are large and produce persistent hemiplegia; (4) more than one episode of acute myocardial infarction, particularly if these occur within a few months; (5) frequently recurring peripheral arterial thrombosis and (6) any combination of acute myocardial infarction, peripheral arterial thrombosis and cerebral arterial thrombosis occurring successively during a period of a year or less. Adequate statistical data support the effectiveness of anticoagulant therapy in most of the afore-mentioned conditions. For acute peripheral arterial or venous thrombosis and pulmonary

(Continued on Page 272)

Diagnosis and Treatment of Local Edema of Lower Extremities

JOHN F. FAIRBAIRN, II, M.D.
Rochester, Minnesota

SWELLING of the lower extremities is a common presenting complaint of the patient to the physician. The patient often fears that the swelling is caused by "dropsy," a fear that induces pronounced but usually needless anxiety in the patient. In addition, a swollen extremity is cosmetically unattractive, a fact that often brings the patient to the physician. Despite patients' fears, the majority of edematous extremities are not associated with serious cardiac, renal or hepatic disease but instead are brought about by local factors and often can be relieved by local treatment. Some of these local factors are summarized in Table I, together with some additional causes of edema. Although each of the local conditions that cause edema of an extremity can, and occasionally does, affect the upper extremities, by far the commonest site of occurrence is in the lower extremities.

Exclusion of the more central or systemic origins of edema, such as congestive heart failure, nephritis or the nephrotic syndrome, cirrhosis or endocrine disorders, leaves five main causative factors for swelling of an extremity, namely physiologic edema, thrombophlebitis, chronic venous insufficiency, lymphedema and lipedema.

Physiologic Edema

Types of edema that may be considered "normal," or "physiologic," are gravitational edema and premenstrual edema. The normal lower extremity that is inactive and dependent often has an accumulation of fluid because of increased hydrostatic pressure. This is commonly seen in persons who travel long distances in trains or automobiles or who sit for hours without activity. People who stand or sit at their work hour after hour without walking about may be similarly affected. Rarely, such persons may be almost incapacitated by the accumulation of edema; however, more often the problem is one of cosmetic deformity or mental anguish rather than of true incapacity. Reassurance of the patient that this swelling does not represent serious disease, and the use of elastic

TABLE I. CLASSIFICATION OF EDEMA OF LOWER EXTREMITIES

Primary, or idiopathic
- Gravitational and physiologic edema
- Lipedema
- Lymphedema

Secondary, or symptomatic
- *Localized or regional disease*
  - Thrombophlebitis
  - Lymphedema
  - Edema of venous stasis
  - Angioneurotic edema
  - Myxedema (pretibial myxedema associated with exophthalmic goiter)
- *Systemic disease*
  - Renal disease: nephritis and nephrosis
  - Myocardial disease: heart failure
  - Hepatic disease: decompensated cirrhosis
  - Endocrine disease: hyperthyroidism; myxedema; aldosteronism; Cushing's syndrome

Treatment-induced edema
- High-salt intake
- Salt-retaining hormones: desoxycorticosterone; cortisone; corticotropin; testosterone; aldosterone; antidiuretic hormone
- Rauwolfia preparations

support and, occasionally, a restricted intake of salt often give these patients help. Edema occurring premenstrually is attributable in part to retention of sodium and water. The precise hormonal abnormality is not known but restriction of fluid and salt sometimes produces remarkable, although rarely complete, relief. These patients do not have edema during the remainder of the menstrual cycle.

Thrombophlebitis

Thrombophlebitis involving only the superficial venous system does not cause edema; however, thrombophlebitis involving the deep system of veins is usually associated with a relatively acute onset of unilateral edema, pain or tenderness in the involved extremity, and the other classic signs of deep venous thrombosis (Fig. 1). With elevation of the leg and use of anticoagulants, the edema subsides within a matter of days. After the signs of acute inflammation subside and the extremity is free of edema, the patient with throm-

Presented at the Symposium on Peripheral Vascular Disease co-sponsored by the Minnesota Heart Association and the Mayo Foundation, Rochester, Minnesota, September 24, 1957.

Fig. 1. Left iliofemoral thrombophlebitis.

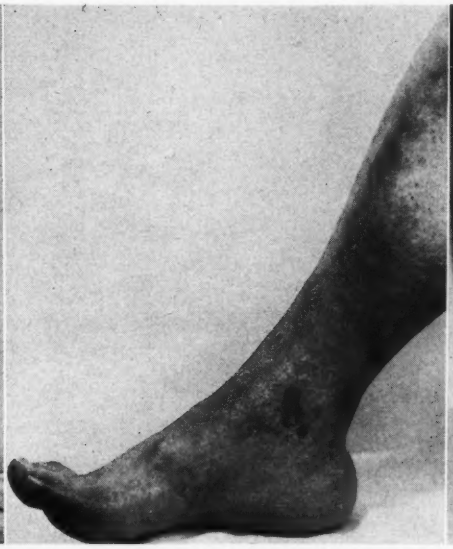


Fig. 2. Chronic venous insufficiency with stasis dermatitis and ulceration.

Fig. 3. Primary lymphedema of left leg, showing "pigskin" appearance.

bophlebitis of the calf or of an iliofemoral distribution should have two elastic bandages applied to the leg before he gets out of bed. These supports should include only that part of the leg from the instep to the infrapatellar region, since it is almost impossible to have a bandage stay in place above the knee. All patients who have iliofemoral thrombophlebitis and most patients with sural thrombophlebitis will have dependent edema immediately after they become ambulatory, and it is unwise to wait to see how much swelling may develop. The patient may become free of edema when adequate elastic support is used for a period of weeks or months.

Chronic Venous Insufficiency

If destruction of the venous valves is extensive and recanalization of the thrombosed vein is inadequate after thrombophlebitis, a tendency for chronic swelling of the extremity may be present. This is chronic venous insufficiency, which most often results from inadequate treatment of the patient during the acute episode of phlebitis and in the period of weeks or months immediately after active thrombophlebitis.

Edema secondary to chronic venous insufficiency may result from involvement of the superficial or the deep venous system or both. The basic defect in patients with edema caused by chronic venous insufficiency is the absence of competent valves, which leads to a pronounced increase in venous pressure in the leg. Normally, the venous pressure at the ankle decreases rapidly with exercise and slowly returns to normal. In a vein without competent valves, the venous pressure does not decrease as much as it does in normal situations and it returns more rapidly to the level present before exercise. With this persistence of increased venous pressure, transudation of fluid is promoted and edema results. An additional factor in the formation of edema may be the relative stasis of blood in the incompetent veins, leading to capillary damage and further promotion of edema. As long as the extremity is drained of all the edema fluid before application of elastic bandages, adequate elastic support almost always controls the edema. Any support is adequate as long as it controls the edema; in my experience, elastic bandages and, occasionally, rubber bandages are needed to control the edema associated with chronic venous insufficiency. However, elastic stockings may control the edema produced by varicose veins.

Some patients with the postphlebitic syndrome or chronic venous insufficiency will have chronic indurative cellulitis and some will go on to have periodic lymphangitis and subsequent lymphatic obstruction, leading to localized or regional lym-

TABLE II. CLASSIFICATION OF LYMPHEDEMA

Noninflammatory
Primary
Praecox
Congenital
Simple
Milroy's (familial)
Secondary
Malignant occlusion
Surgical removal of lymph nodes
Pressure
X-ray and radium therapy
Inflammatory
Primary (single episodes, recurrent acute or chronic episodes)
Secondary (single episodes, recurrent acute or chronic episodes)
Venous stasis
Trichophytosis
Systemic disease
Local tissue injury

phedema; more frequent than these complications are the usual sequelae of chronic venous insufficiency, namely stasis pigmentation, dermatitis and ulceration (Fig. 2). The majority of these complications can be prevented by the avoidance of chronic edema in an extremity. If the patients are alerted to these late complications and understand that elastic support is used for the purpose of avoiding chronic edema in order to prevent subsequent ulceration, cellulitis and lymphangitis, they will be more likely to be careful about using elastic bandages or stockings.

Lymphedema

Lymphedema is a relatively uncommon condition that is confused most often with chronic venous insufficiency; if the lymphedema is acute in onset, it may be confused with deep venous thrombosis. Although there are many causes of lymphedema (Table II), there appears to be a common mechanism of production.

Stasis of lymph occurs initially because of obstruction to the normal flow of lymph. This obstruction may be caused by inflammation, congenital lymphangiectasis or malignant invasion. With subsequent thrombosis of lymphatic vessels, proliferation of fibroblasts occurs in the lymph, which is an excellent culture medium for tissue, and with the destruction of valves in the lymphatic vessels, new but incompetent lymph channels appear and the same cycle recurs. The region eventually becomes edematous without signs of venous disease. The lymphatic systems of the leg are divided into deep and superficial portions by the deep muscular fascia. It is the superficial system that becomes involved mainly in lymphedema; the skin is thickened, and the hair follicles become prominent, giving the appearance commonly referred to as "pigskin" (Fig. 3). Early in lymphedema, the swelling is soft and pittable, and it often recedes completely on elevation of the extremity. Later, the tissues become more and more indurated and less of the swelling disappears with elevation; some tissue hypertrophy occurs, which also increases the size of the leg. The usual site for lymphedema is in one lower extremity, including the foot, although both legs may be involved. In the congenital type, an arm or even the face may be lymphedematous.

In treating lymphedema, it is important to attempt to reduce the swelling to a minimum by continuous twenty-four-hour elevation of the leg, which is done best in the hospital. After one to three days of elevation, all the swelling that can be eliminated usually will have left. The patient is then instructed in the proper application and use of an adequate elastic support. A Pará gum-rubber bandage is the most effective type of support, although it is heavy and often uncomfortable, especially in warm weather. A lisle stocking, worn under the rubber bandage, gives some protection against dermatitis and skin irritation from excessive perspiration. With continued use of this support, the extremity will not continue to enlarge or its rate of enlargement may be slowed. The patient should be warned that the lymphedematous extremity is a frequent site for infection or lymphangitis, that such infection may produce further enlargement, and that prompt antibiotic treatment of the infection is necessary. Trichophytosis should be treated and controlled, since such fungous infections may provide sites of entry for bacteria. The surgical treatment of lymphedema consists in wide excision of lymphedematous subcutaneous tissue. Its use is reserved for massively enlarged limbs, and the patient who elects surgical intervention often trades a swollen limb for a badly scarred and still abnormal-appearing extremity.

Again, as in chronic venous insufficiency, the patient should be thoroughly instructed and oriented as to the need for adequate elastic support and the methods of prevention and treatment of lymphangitis. Even with enthusiastic encouragement by the physician, a large number of patients discard their bandages and their legs progressively enlarge, becoming subject to the complications of untreated lymphedema.

Fig. 4. Typical appearance in lipedema. Note absence of involvement of feet.

Fig. 5. Pretibial myxedema.

Lipedema

Lipedema means the deposition of excessive amounts of fat in the legs, with secondary orthostatic edema. This condition is almost always bilateral and affects women almost exclusively. A family history of similar fatty swelling may be present. The cause of this unusual fatty accumulation is not known. It may be present in childhood and may be exaggerated by recent gain in weight, yet reduction of weight does not appear to alter the basic appearance of the legs. The upper part of the trunk and the upper extremities usually appear normal, with an accumulation of fat about the hips and extending into the thighs and legs but not involving the feet (Fig. 4). The skin is normal in appearance but is often hypersensitive. Pitting edema usually cannot be demonstrated, because the collections of extracellular fluid lie in the interstices between fatty deposits; however, some patients may note pitting edema especially in warm weather or when they are on their feet for long periods.

Rarely, lipedema may involve both arms.

The treatment consists mainly of reassuring the patient that this condition does not represent any serious disease. Elastic supports occasionally help to prevent accumulation of fluid, but the patient often cannot tolerate tight bandages or stockings because the skin is tender.

Other Types of Local Edema

Any patient who manifests edema of obscure cause or who notes an unexplainable increase in swelling of the leg should be closely questioned as to the ingestion of medicaments, because drug-induced edema may explain this swelling. The Rauwolfia drugs, hydralazine (apresoline) hydrochloride and cortisone or other adrenal steroids are common offenders in this regard.

An unusual type of local edema may occur only in the pretibial region or on the dorsum of the foot. This is termed "localized" or "pretibial" myxedema (Fig. 5). However, this terminology is poor, since the condition bears no relationship to the presence or absence of generalized myxedema; instead, it is always seen in patients with exophthalmic goiter. It is usually a self-limited process that disappears over the course of years. Such swelling might be mistaken for lipedema, but the peculiar localization to the pretibial region and the foot is not seen in lipedema.

(Summary on Page 277)

A New Concept in the Surgical Treatment of Aortic Insufficiency

J. J. GARAMELLA, M.D., J. G. ANDERSEN, M.D.
R. OROPEZA, M.D., N. K. JENSEN, M.D.
L. J. HAY, M.D., R. NAIDU, M.D.
Minneapolis, Minnesota

ALTHOUGH stenotic lesions of the aortic valve were surgically attacked as early as 1913 by Tuffier,[1] who attempted dilatation by invagination of the aortic wall, little was done toward the sugical correction of aortic regurgitation until Campbell[2] in 1950 and Hufnagel[3] in 1951 introduced prosthetic valves in the descending portion of the aorta. Other methods tried experimentally and clinically for the control of aortic regurgitation include transplantation of homologous aortic valves,[4,5] injection of sclerosing solutions around the aortic annulus,[6] pericardial pedicles[6] and vein grafts,[5] organic prostheses,[7] and circumferential, pursing sutures of the aortic annulus.[6,8] Supracoronary and subcoronary prosthetic valves have also been described.[6,9,10,11] Although placement of a prosthetic valve in the descending aorta has received extensive clinical trial by Hufnagel, limitations of the method are: (1) the partial control of regurgitation because of the distal location of the artificial valve; (2) the relation of the coronary arteries to the new aortic valve is reversed; (3) a permanent foreign body is introduced into the blood stream with the possible sequelae of trauma to blood cellular elements and thrombus formation. The circumclusion technique introduced by Bailey was abandoned by him after forty-three clinical trials.

Inasmuch as acquired forms of aortic insufficiency are characterized by a loss of valve substance and dilatation of the aortic annulus,[12] an operation was designed to alter the pathologic anatomy, namely, to permanently reduce by one third the circumference of the dilated aortic valve ring by totally excising the non-coronary aortic cusp and its corresponding segment of aortic wall, converting the tricuspid aortic valve to a bicuspid valve (Fig. 1). In so doing, improved coaptation of the two remaining damaged coronary cusps is achieved. Accordingly, the normal relationship between the reconstructed aortic valve and coronary arteries is retained and no foreign body is introduced into the vascular system.

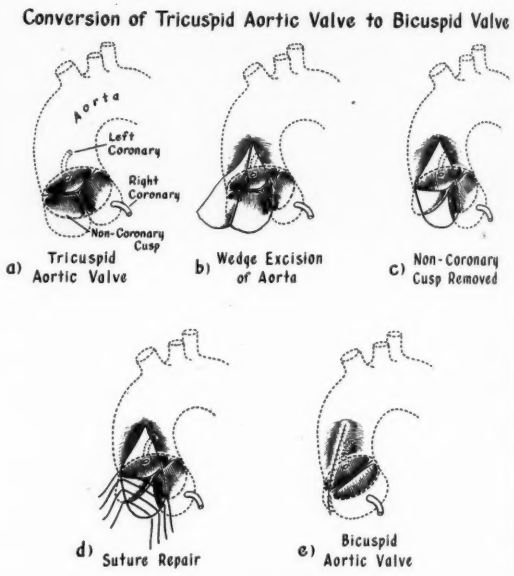


Fig. 1. Schematic drawings showing method of converting the tricuspid aortic valve to a bicuspid valve by total excision of the non-coronary aortic cusp and a corresponding segment of the aortic wall. Procedures were done under direct vision employing a pump-oxygenator and elective cardiac arrest.

In order to test this concept, experimental studies were performed on dogs to determine whether or not conversion of the tricuspid aortic valve to a bicuspid valve was compatible with survival, and secondly to determine whether or not significant degrees of dynamic aortic stenosis and/or aortic insufficiency were produced. In effect, a severe degree of aortic insufficiency is produced by total excision of the non-coronary

Presented at the meeting of the Minnesota Surgical Society, November 1, 1957, Minneapolis, Minnesota.
From the Jay Phillips Research Laboratory, Mount Sinai Hospital and the Department of Surgery, University of Minnesota, Minneapolis, Minnesota.
Supported by U.S.P.H. Grant No. H-2610 and Cardiac Research Committee, Minneapolis, Minnesota.

aortic cusp and this is surgically corrected by the technique described. A defect of more than one third of the posterior cusp has been found intolerable in experimental animals.[13] Operative procedures were performed under direct vision with cardiac by-pass employing an extracorporeal pump-oxygenator[14] and elective cardiac arrest.[15]

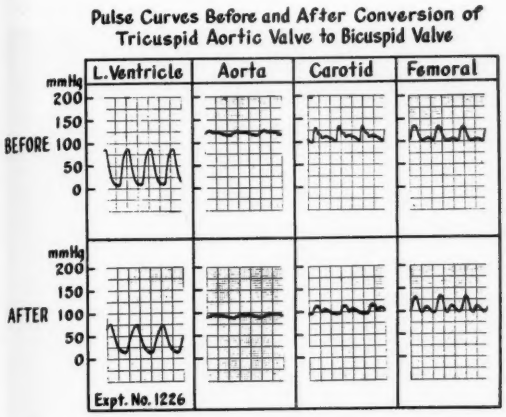


Fig. 2. Arterial pulse curves taken before and after conversion of the tricuspid aortic valve to a bicuspid valve show slight elevation of the end-diastolic pressure in the left ventricle, absence of a gradient across the aortic valve and dicrotic notches and dicrotic waves in the aortic, carotid, and femoral pulse tracings. The dicrotic notch and wave are representative of aortic valve closure.

Results

In twenty consecutive studies there were eleven acute survivors. Seven animals are long-term survivals (four to six months). Additional chronic survivors not included in this analysis have been obtained, however.

During our early experience with the method seven of nine acute postoperative deaths were due to severe dynamic aortic insufficiency as evidenced by absence of the dicrotic notches and dicrotic waves in the arterial pulse curves in the postoperative period. The dicrotic notch and dicrotic wave are representative of aortic valve closure.[16-19] A more deliberate coaptation of the newly formed posterior commissure of the bicuspid valve in the last nine of the twenty studies was attended with consistent post operative dicrotic arterial pulse curves and improved animal survival, seven acute survivors and two preventable deaths (hemothorax and tracheal obstruction). Previous postoperative studies[20] including analyses of arterial pulse curves (Fig. 2), measurements of the duration of the ejection phase of systole, retrograde aortography (Fig. 3), and transvalvular pressure determinations showed no significant degrees of aortic stenosis and/or aortic insufficiency in the surviving animals.

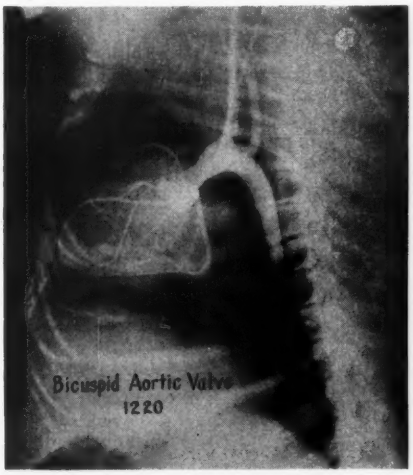


Fig. 3. Postoperative retrograde aortogram showing: (a) bicuspid nature of a aortic valve, (b) surgical narrowing of aorta, (c) coronary artery filling, (d) absence of dye in the left ventricle. Arterial pulse curves showed dicrotic notches and dicrotic waves.

To determine the feasibility of this operative procedure in clinical aortic regurgitation a series of photographs were prepared from an autopsy specimen obtained from a patient that succumbed of acquired aortic insufficiency. These are shown in Figs. 4, 5, 6, 7 before and after conversion of the tricuspid aortic valve to a bicuspid valve. The anatomic reduction of the regurgitant site is apparent following the operative procedure.

Other preliminary investigations showed that if the aortic wall was reduced by one third without excision of the corresponding non-coronary cusp, there is, in effect, a herniation of the non-coronary cusp below the two coronary cusps in which case it does not appear to contribute to the function of the refashioned valve and probably detracts from it.

Isolated disease of the non-coronary cusp (as following trauma or congenital perforation, for example) seemingly would be suited for this type repair. Possible clinical application for other acquired regurgitant pulmonic lesions is suggested.

Summary

A new concept in the surgical treatment of aortic insufficiency is introduced. The surgical method consists of plastic revision of the tricuspid aortic valve to a bicuspid valve by total excision of the noncoronary aortic cusp. Experimental data and a preliminary pathologic study support the feasibility of the method.

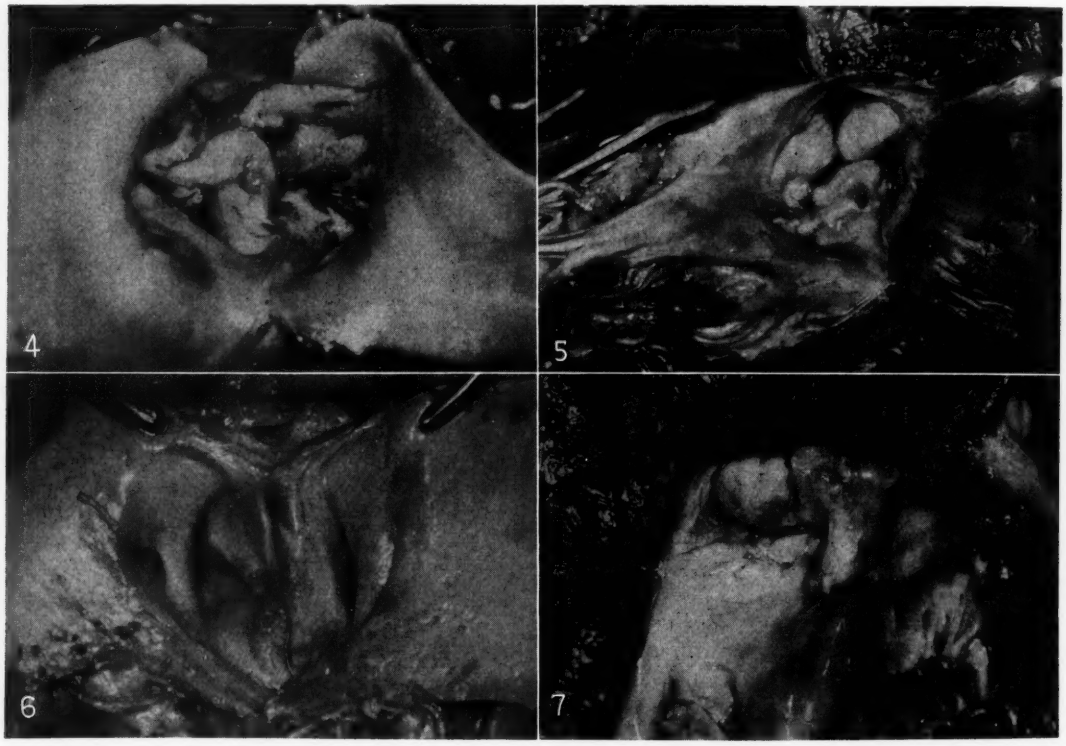


Fig. 4. An autopsy specimen from a patient dying of aortic regurgitation shows the insufficient aortic valve viewed from above and posteriorly. Note the distortion, thickening and shortening of the aortic cusps. The central defect causing aortic regurgitation is evident. The loss of cusp substance precludes complete coaptation. Dilatation of the aortic ring is not a conspicuous feature of this specimen.

Fig. 5. Insufficient aortic valve viewed from below, the ventricular side, showing the central defect causing regurgitation. The posterior, non-coronary cusp occupies the lower part of the valve orifice. A rim of calcification is noted on the right.

Fig. 6. The incompetent aortic valve seen in Figs. 4, 5 is viewed from above following plastic revision with total excision of the non-coronary aortic cusp. The valve is now bicuspid. The circumference has been reduced by one-third. The remaining coronary aortic cusps appear to coapt well. The left coronary ostium is visualized to the left.

Fig. 7. The incompetent aortic valve seen in Figs. 4, 5 is viewed from below, ventricular side, following plastic revision. The non-coronary aortic cusp has been excised. The newly formed bicuspid valve appears to coapt well. Sutures in the line of repair are evident.

References

1. Tuffier, T.: Etat actuel de la chirurgie intrathoracique. Tr. Internat. Cong. Med., London, 1913. Surgery, 2:249, 1914.
2. Gampbell, J. M.: An artificial aortic valve. Preliminary report. J. Thoracic Surg., 19:312, 1950.
3. Hufnagel, C. A.: Aortic plastic valvular prosthesis. Bull. Georgetown Univ. M. Cent., 4:128 (Feb.-March) 1951.
4. Lam, C. R., Aram, H. H., Munnell, E. R.: An experimental study of aortic valve homografts. Surg. Gynec. & Obst., 94:129, 1952.
5. Bailey, C. P., Glover, R. P., O'Neill, T. J. E., Ramirez, H. P.: Experiences with the experimental surgical relief of aortic stenosis. J. Thoracic Surg., 20:516, 1950.
6. Bailey, C. P.: Surgery of the Heart. Philadelphia: Lea and Febiger, 1955.
7. Litwak, R. S., Gadboys, H. L., Scott, G. B., Ferrarar, J. F.: Surgical approach for stenotic lesions of the semilunar valves by excision and cusp replacement under direct vision. J. Thoracic Surg., 24:165 (August) 1952.

(Continued on Page 277)

A New Antirheumatic Steroid

Preliminary Report

PAUL J. BILKA, M.D.
JAMES C. MELBY, M.D.
Minneapolis, Minnesota

ALMOST immediately following the demonstration of the physiologic effects of cortisone in human patients,[1] and the subsequent correlation of the chemical structure of related steroid compounds with their physiologic action,[2,3] a sustained effort has been going on in many centers to develop and test compounds of maximal therapeutic effectiveness but with a minimum of the adverse side effects.[4] The major "desirable" effect of these compounds is their anti-inflammatory action. This property, which has been referred to by Selye as the anti-phlogistic[5] effect, appears to be non-specific regarding the type of inflammation affected and has extended the clinical usefulness of the compounds to such diverse disorders as rheumatoid arthritis, ulcerative colitis, iritis, pemphigus and certain specific infectious diseases.[6,7]

The major "undesirable" effects relate to (1) pituitary and adrenal cortex suppression, (2) Sodium retention and potassium loss—the mineral-corticoid effect, (3) increased protein catabolism, or the anti-anabolic effect which may explain the osteoporosis, the altered reaction of tissue to healing and infection,[8] and the high incidence of peptic ulcer, and (4) collagen vascular disease[9] or so-called hypercortisonism.[10] Thus far, the only undesirable effect that has been significantly altered with the newer steroids has been the marked lessening of sodium retention and potassium loss with the delta-1 steroids prednisone and prednisolone. However, along with the increased antirheumatic potency of these new compounds, a comparable intensification of the glucocorticoid and other effects has occurred and the major hazards of steroid therapy remain.

From the department of medicine, University of Minnesota, Minneapolis, Minnesota.

The 6-methylprednisolone used in this study was supplied as Medrol by Dr. H. C. Peltier of the Upjohn Company, Kalamazoo, Michigan.

Method

We wish to report our clinical findings in a group of ambulatory rheumatoid arthritic patients who were studied critically in an attempt to compare a new steroid, 6-methylprednisolone (or $\Delta^{1,4}$ 6 α-methylhydrocortisone with the more usually employed corticoids.

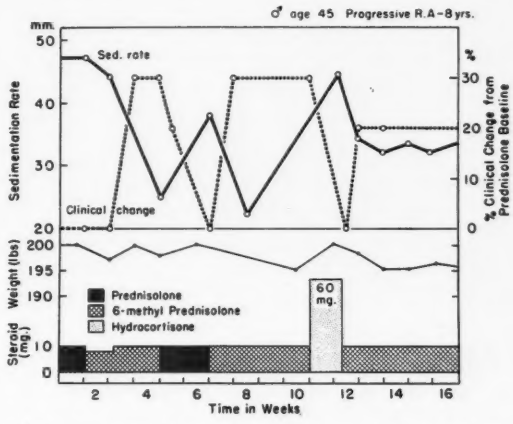


Fig. 1. Comparison of corticoids used in treating a patient with rheumatoid arthritis.

Twenty patients who were being maintained on prednisolone were given 6-methylprednisolone in doses of 2 to 10 mg. per day. The usual procedure was to vary the dosage of the new drug until a clinical level of control was obtained that was equal to that which the patient experienced on his maintenance prednisolone dosage. The patient was them returned to the original prednisolone medication. In eighteen cases, the new medication was given again as a check on the first trial; in several patients, more than two trials were given. Objective joint examinations were performed with measurement of swelling, tenderness and range of motion. The patients were seen at weekly intervals and recordings were made of

weight, blood pressure, hemoglobin, and sedimentation rate.

Results

The graphic record of one patient is presented in Figure 1. In Table I, the findings in the twenty patients are summarized. Two patients required the same dosage of 6-methylprednisolone as prednisolone for a given degree of improvement. The remaining eighteen patients, or 90 per cent, required only 50 to 75 per cent of the prednisolone dosage. In seven cases, the ratio of prednisolone to 6-methylprednisolone was 4:3, in nine cases it was 3:2 and in two cases it was 2:1.

TABLE I. 6 METHYLPREDNISOLONE (M) FINDINGS IN TWENTY CASES
As compared with Prednisolone (P)

Case	Duration of Therapy in Weeks	Relative Anti-Rheumatic Potency	Weight Change and Other Effects
1	5	7.5 mg. P= 5 mg. M	Loss 4 lbs.
2	14	15 mg. P=10 mg. M	Loss 2 to 5 lbs; less GI distress.
3	10	10 mg. P=7.5 mg. M	Loss 2 to 4 lbs; better appetite; "more drive."
4	10	7.5 mg. P= 5 mg. M	Loss 3 to 7 lbs; initial epigastric distress.
5	4	6 mg. P= 5 mg. M	Loss 2 lbs; severe headache on second trial.
6	6	6 mg. P= 4 mg. M	Weight same; "more alert."
7	6	4 mg. P= 2 mg. M	Loss 1½ to 4 lbs.
8	4	5 mg. P= 4 mg. M	Loss 4½ lbs.
9	4	6 mg. P= 4 mg. M	Loss 1 lb.
10	2	6 mg. P= 4 mg. M	Loss 2 lbs.
11	1	7.5 mg. P= 5 mg. M	Loss 1 lb.
12	4	8 mg. P= 8 mg. M	Loss ¾ lb.
13	2	5 mg. P= 4 mg. M	Loss ¾ lb.
14	4	5 mg. P= 5 mg. M	Loss 3 lbs.
15	3	5 mg. P= 4 mg. M	Loss 5 lbs.
16	1	5 mg. P= 4 mg. M	Loss ½ lb.
17	3	6 mg. P= 4 mg. M	Loss 3 lbs; "quicker effect and more even."
18	2	5 mg. P= 3 mg. M	Weight same.
19	6	6 mg. P= 4 mg. M	Loss 3 lbs.
20	3	6 mg. P= 5 mg. M	Weight same.

Three patients showed no weight difference on the two medications and two patients lost less than 1 pound in body weight on taking 6-methylprednisolone. Nine patients lost from 1 to 3 pounds and six patients lost from 3 to 5 pounds. Most patients were aware of increased urination, and several who had clinical edema noticed less ankle-foot swelling. The weight loss usually occurred in the first three days but in some patients a slower and steady weight loss was observed. Except for the diuresis, no other striking clinical differences were observed. Several patients with facial "mooning" retained this feature on 6-methylprednisolone. The period of observation has been too short to draw any conclusions concerning the other major side effects of this new compound.

Comment

It has been postulated that alterations in metabolism of the steroid compounds may account for the altered biological effects. Liddle and Richard reported that 2-methylhydrocortisone is removed from the plasma more slowly than hydrocortisone.[11] Prednisolone is excreted in the urine unchanged to a much greater extent than is hydrocortisone which occurs in the urine mainly as a reduced and conjugated metabolite.[12] An effort to assess this alteration in metabolism was made by the intravenous administration of hydro-

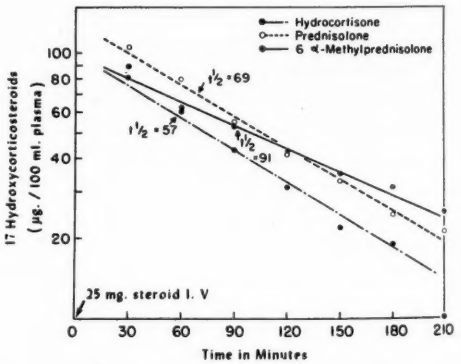


Fig. 2. Plasma biological half-lives of hydrocortisone, prednisolone and 6-methylprednisolone (Medrol) in the dog.

cortisone, prednisolone and 6-methylprednisolone in dogs. After the injection of 25 mg. of these steroids, blood specimens were obtained at thirty-minute intervals and analyzed for 17-hydroxy-corticosteroids by the method of Silber and Porter. The mean plasma biological half-lives were calculated from these data. The plasma biological half-life for hydrocortisone was fifty-seven minutes; for prednisolone, sixty-eight minutes; and for 6-methylprednisolone, ninety-one minutes as, graphed in Figure 2. The prolonged plasma biological half-life of 6-methylprednisolone can be correlated with recent studies which show that this compound is resistant to attack by liver enzymes and hence is slowly metabolized as compared with the parent steroids.[13] Reported experimental data in rats indicates that the new compound, when compared with prednisolone, was two times as potent on the anti-inflammatory test, about three times as potent on glycogen deposition assay, and in contrast to prednisolone this steroid acted as a diuretic and natri-uretic agent.[14]

Summary

A new antirheumatic steroid, 6-methylprednisolone, was compared with prednisolone in twenty patients with rheumatoid arthritis. The new compound appears to be about 25 per cent more potent than prednisolone and has mild diuretic properties. No other striking differences from the usually employed steroids were seen in this preliminary study. The diminished rate of removal of 6-methylprednisolone from the plasma of dogs, as compared with prednisolone and hydrocortisone, may relate to the enhanced clinical effectiveness observed.

References

1. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: Effects of cortisone acetate and pituitary ACTH on rheumatoid arthritis, rheumatic fever and certain other conditions: A study in clinical physiology. A.M.A. Arch. Int. Med., 85:545-666 (April) 1950.
2. Polley, H. F., and Mason, H. L.: Rheumatoid arthritis: Effects of certain steroids other than cortisone and of some adrenal cortex extracts. J.A.-M.A., 143:1474-1481 (Aug. 26) 1950.
3. Fried, J.: The Relation of chemical structure to biological activity of adrenal-cortical steroids. Bull. Rheumat. Dis., 6:111-112 (May) 1956.
4. Black, R. L., Yielding, K. L., and Bunim, J. J.: Observations on new synthetic antirheumatic steroids and critical evaluation of prednisone therapy in rheumatoid arthritis. J. Chron. Dis., 5:751-769 (June) 1957.
5. Selye, H.: Recent Progress in Hormone Research. 8:117-142. New York: Academic Press, 1953.
6. Lukens, F. D. W.: Medical Uses of Cortisone. New York: The Blakiston Company, 1954.
7. Spink, W. W.: Adrenocorticotropic hormone and adrenal steroids in the management of infectious diseases. Ann. Int. Med., 43:685-701 (Oct.) 1955.
8. Howell, D. S., and Ragan, C.: The course of rheumatoid arthritis during four years of induced hyperadrenalism (IHA). Medicine, 35:83-119 (May) 1956.
9. Bunim, J. J.: Clinical uses and hazards of adrenal steroids and their analogues in the management of rheumatic diseases. Bull. New York Acad. Med., 33:461-473 (July) 1957.
10. Slocumb, C. H., Polley, H. F., Ward, L. E., and Hench, P. S.: Diagnosis, treatment and prevention of chronic hypercortisonism in patients with rheumatoid arthritis. Ann. Int. Med., 46:86-101 (Jan.) 1957.
11. Liddle, G., and Richard, J. E.: 2-Methyl Hydrocortisones: A new series of steroids with enhanced potency and prolonged action. Science, 123:324-235 (Feb. 24) 1956.
12. Slaunwhite, W. R., Jr., and Sandberg, A. A.: The metabolism of the 1-dehydro-17 hydroxy-corticosteroids in human subjects. J. Clin. Endocrinol., 17: 395-406 (March) 1957.
13. Glenn, E. M., Stafford, R. O., Lyster, S. C. and Bowman, B. J.: Relation between biological activity of hydrocortisone analogues and their rates of inactivation by rat liver enzyme systems. Endocrinology, 61:128-143 (Aug.) 1957.
14. Lyster, S. C., Barnes, L. B., Lund, G. H., Menzinger, M. M., and Byrnes, W. W.: Adrenal corticoid activities of 6-methyl-delta 1-hydrocortisone. Proc. Soc. Exper. Biol. & Med., 94:159-162 (Jan.) 1957.

63 S. 9th Street
Minneapolis 2, Minnesota

PERIPHERAL VASCULAR DISEASES

(Continued from Page 240)

discussion on a note of pessimism. However, I have lived through the era of intermittent suction and pressure and intermittent venous occlusion. The machines used for these purposes now belong quite properly in a medical museum. The medical treatment of hypertension, the proper use of anticoagulants, and the development of arterial surgery are great and thrilling accomplishments, as are other methods of treatment which I have mentioned. When one views the general field of peripheral vascular diseases, he can only be optimistic.

Editorials

JOHN F. BRIGGS, M.D.
ARTHUR H. WELLS, M.D.
HENRY G. MOEHRING, M.D.

INFANT FEEDING

The Evaporated Milk Chapter

That more than two-thirds of the babies born in U. S. hospitals are discharged on a bottle formula of some kind was disclosed in a recent survey. In these formulas evaporated milk is being prescribed more than all other forms of cow's milk combined, including the special proproprietary infant feeding preparations.

It was not always thus. Prior to 1929, the medical literature contained infrequent reports on the use of evaporated milk in infant feeding. In that year, two great investigators in infant nutrition, independently and coincidentally, published the results of their studies on large numbers of babies, Brennemann, in the February 2 issue of the *Journal of The American Medical Association* and Marriott in the March issue of *Archives of Pediatrics.*

Brennemann reported his observations in particularly glowing terms.—"The result was all that has been claimed and all that could be hoped for, and again such as I had never seen before with any other food. . . . The gain in weight was better than before—sometimes truly amazing—and, I feel sure, as good as if the babies had been on breast milk." Marriott reached similar conclusions based on evaporated milk formula feeding to 752 young infants.

Doctor Brennemann had long been concerned with the curd problem when ordinary cow's milk was used in the feeding formula. He observed that with evaporated milk, under conditions simulating those existing in the infant stomach, the casein coagulates not in a cheese-like mass, but in a soft semi-fluid condition comparable to the protein coagulum from human milk. He believed that this reduction in curd tension removed the most important source of difficulty that arises from the ingestion of formulas prepared from cow's milk; and this is generally accepted in the medical profession at this time. Certainly, all products that are promoted as the basis for formula construction stress the point of curd tension.

During the 1930's, numerous other clinics conducted infant feeding studies, comparing the nutriture of infants on evaporated milk formulas with other forms of cow's milk and even with human milk. Mineral and nitrogen retentions were determined. Fat digestibility experiments were performed, and the growing list of vitamins, to which so much attention was being given during that period, came under the scrutiny of the laboratory technologists.

As expected, they found that some of the vitamins were reduced appreciably percentagewise in the technique of converting raw cow's milk into evaporated milk, but there was no loss that would indicate the institution of precautionary measures other than had been practiced before, such as the routine administration of vitamins C and D. On the other hand, the researchers observed that certain of the nutrients were even better utilized from evaporated milk formulas than from formulas prepared from other forms of milk. The apprehension which had existed before, which actually materialized as a prejudice against "canned milk" was gradually dispelled.

In the process of producing evaporated milk from raw cow's milk sufficient heat is applied to protect it against spoilage. This is known to be the principle factor that brings about the favorable change in the casein. Homogenization also is a factor in lowering curd tension, though a minor one.

Actually the homogenization process is applied for the purpose of reducing the fat globules to such size that they do not "cream off" during the shelf life of the can of milk. But it happens also to add a nutritional advantage; as the milk fat in this highly homogenized form presents a greater surface to the fat digestive enzymes. The milk fat becomes more readily digested, an effect especially important in difficult feeding cases.

The ease with which the infant digests and metabolizes the nutrients in the milk has very likely contributed to the success that has been experienced in many medical centers with formulas prepared by merely diluting the milk with water, and without addition of carbohydrate.

Among other factors that have advanced the use of evaporated milk in the preparation of the

formula have been the observed reduced allergenicity of the protein composite, especially the whey proteins, and the universal fortification of the product with vitamin D. But each of these subjects could easily be made a separate "chapter" in the infant feeding story. Also there is an extensive literature reporting the widespread and successful use of evaporated milk as the basis for special formulas for prematures.

That the advantageous feeding of evaporated milk is not limited to the neonatal period has been demonstrated in a number of studies where it has been the single form of milk given children for drinking throughout the growing years. This is of particular consequence in areas where there is an inadequate supply of good quality low cost market milk.

And there are a number of practical reasons why the medical profession has accepted evaporated milk as a desirable form of cow's milk for child feeding—uniformity of product from day to day and city to city, and its universal availability at relatively low cost are among the contributing factors. Also important to many physicians is the fact that it lends itself to individual formula modification.

In the United States and in certain other parts of the world there has been a striking reduction in infant mortality in recent years. The growing use of evaporated milk, especially vitamin D evaporated milk has been credited with being a contributing factor. Other factors of equally great importance, of course, have been—improved medical care, better home sanitation and an increasing understanding through research of infant digestion and metabolism.

Present day medical literature contains fewer contributions on routine infant feeding techniques than formerly. The factors that make for successful formula feeding are quite well established. Infant disorders are found more likely to arise from causes other than food. However, in the feeding of the disordered infant mechanism there are gaps in our present knowledge. The cow's milk formula does differ from human milk in a number of respects—more protein, more electrolyte, a different fat composition and Ca:P ratio. Just how significant are these differences in feeding the sick baby is quite properly the subject of intensive clinical study.

It is well that the doctor does not need to give as much attention to the feeding of the normal baby as he did thirty years ago. Physicians can now become really "physicians for the young of the race instead of highly paid nannies," as Dr. Alton Goldbloom recently put it.

FRANK E. RICE, Ph.D.

TRENDS IN MEDICINE

Let me assume for the moment that our fictional patient has completed his check-up. His doctor, an impossible paragon if he has investigated all facets of our patient's physical, mental and spiritual health, sums up:

"There is not anything fundamentally wrong with you. Your heart, lungs, intestinal and urinary tracts are in excellent condition. Your electrocardiogram is normal as are your numerous blood tests. True, your blood pressure has been somewhat higher than the average for your age ever since your recent promotion, and I cannot approve of your working so intensely. I do appreciate that you will gain more weight if you stop smoking, but this is not a sound reason for your smoking to excess. The fact that you feel you need the three drinks before dinner indicates more tension than you admit, as does your restless, non-refreshing sleep. I was sorry to hear of your father's untimely death from a stroke, and I am certain that your brother's coronary worries you. These two vascular accidents in the male side of your family do not mean that you will have one too, but they should be added incentives to keep you in the healthiest possible condition. I strongly urge that you lose about 15 pounds and reduce your tobacco consumption by half. I also urge that you get regular exercise and develop other interests besides your work. In fact the best way to start on this program would be to take several weeks' vacation at once."

This is not an atypical summary of an intelligent physical appraisal, nor is it lacking except in concrete recommendations. Partly because I myself have made this speech so often in my practice without being able to go further I was induced to leave my practice for the Aspen project.

The Aspen Institute program is not a new idea, for the basic principles go back to Greek and Roman days. Nor is there any mystery or fetishism in the program. It is neither an intellectual bull-session nor a bake and massage center. Rather it is an effort to combine organized conversation with physical rehabilitation. Both mind and body need stretching beyond the threshold of stimulation if they are to grow. Bad habits

Third in a series of editorials on Trends in Medicine.

in eating, lack of exercise, lazy reading, like all bad habits, are hard to eliminate. It is so obvious however that many of our most useful, productive, and creative citizens are hell-bent on destroying themselves by abuse or disuse of body and mind that the Aspen project can be genuinely classed as a venture in preventive medicine of the highest type.

The Aspen idea, conceived ten years ago by Walter Paepcke, comprises two parts—the Seminars or discussion groups which have been in operation for seven years—and the Health Program which began only in 1957. The marriage of the two under one roof—the Aspen Institute—was obviously logical and desirable, and was accomplished last summer. There is therefore one program which includes reading, discussion, planned exercise, various types of physiotherapy, and relaxation. Both the reading and the exercise are graduated, becoming more difficult as the days pass. The spirit is tended by periods of rest, and the beautiful surrounding scenery of mountains, forests, lakes and streams is naturally designed for contemplation and refreshment. Regularity in hours, various outdoor activities, the best in music, and adequate sleep round out the program.

The two-week course is an exciting experience which has converted even the most skeptical. It is difficult to describe without becoming fulsome. The entire program, conducted away from the stress and routine of one's daily life, is ideally suited to enable an individual to change his pattern. We believe that such a change, properly directed, may become permanent. Thus far about half of the "alumni" seem to have retained real benefit, and we hope have prolonged their lives and increased their productivity. The program is ideal for the patient mentioned in my opening paragraph, and it is the fundamentally well man who is however tending to destroy himself whom we are trying to save.

"Mens sana in corpora sano" could be our motto, if we were to have one. Instead, let us say that we are trying to prevent illness by developing better habits in mental and physical fields, and by increasing awareness of the inseparable relationship which exists between body, mind and spirit. This is the essence of the Aspen project, and it is this which makes it so bold and imaginative a venture in the field of preventive medicine.

CHARLES S. HOUSTON, M.D.
Aspen, Colorado

MEDICAL LIBRARIANS: WHAT DO THEY DO?

Sooner or later in the life of every medical librarian, some interested or curious person will ask, "*What* do you do all day with your time?" Or some one will stop at the door and say in a shocked voice, "Is this where you *sit* now?" Because the idea of medical librarianship as a career has not been as widely publicized as other fields of librarianship or as other professions associated with the care of sick in hospitals, the profession is evaluated negatively by the misinformed. To them a librarian appears to do nothing but sit at a desk keeping a custodial eye on the books and occasionally taking one off the shelf and putting it back again for a seldom-seen patron. Actually, the work is dynamic, often it is very exciting, and always, it is most satisfying, intellectually.

However, what a medical librarian does depends, first, on two factors: on her academic and personal qualifications and on what the institution which employs her expects her to do. If those who employ her do not realize that she has clearly defined functions within her own field, one of several conditions may exist. She may be selected on the basis of her ability to do "light typing," or she may be a former member of an active staff or faculty who is assigned to the library as the first plank to retirement. Or again, a person may be chosen to fill this position who has many extra-librarian aptitudes, that is, one who is readily convertible into a secretary, a public relations person or a handy man to manipulate the mechanical gadgets, the tape recorders, the slide projectors, and the movie machine. Unless a librarian is chosen with sound academic and personal qualifications, the type of work done in the medical library will be inferior and the library will make slow progress, if any.

Minimal academic qualifications for medical librarianship include a bachelor's degree with basic work preferably in languages, literature and the biological sciences. An additional year of study in an accredited library school is a requisite. Courses in medical terminology, bibliography and in medical librarianship are also essential preparation for the profession. The latter courses if taken in a university approved by the Medical Library Association prepares a librarian for Grade I Certification by the Association. Librarians may qualify for Grades II and III Certification by

taking internships, again at approved universities, and by doing graduate work, both in librarianship and in medical subject fields. The purpose of certification is to raise the standards of the profession, to form criterion by which professional knowledge of the librarian may be judged and to give those who employ librarians a reliable guide for their choice.

As to personal qualifications the medical librarian must have those which make her adaptable to her specialized type of work. Medical librarians writing in their own literature single out essential traits. She must have a mind that prefers organization to disorder, a liking for books and for working with people, initiative, curiosity, imagination, a sense of humor, a strong constitution. Miss Mildred Crowe, librarian at the Alabama Medical Center says, "She should be a saint, a scholar, a teacher, and a technician."

The field of medical librarianship is a complex one. Much of what a librarian will do depends also on the size and type of the affiliating institution: agency, society, school or industry. While the basic principles of librarianship are the same in all types of special libraries, duties and services will vary according to the aims and objectives of the parent affiliation. The needs of clientele will be quite different in the National Library of Medicine, than they will be in a pharmaceutical research library, a medical society's library or in the library of a teaching or non-teaching hospital.

Other factors that affect the extent and the type of work a librarian does are: the size of the budget allocated to the library, the distance the library may be from larger and more comprehensive collections of the same subject matter and the needs or demands of its clientele, for in libraries as in all institutions with commodities, the user creates the demand.

The final word on the questions, "What do you do with your time?" depends, in great measure on the resourcefullness, imagination and judgment of the individual librarian. One person's remark, "I have never seen a medical librarian who is not happy in her work," is really the heart of the whole matter. Where work is done whole-heartedly in the spirit of dedication, there is practically no limit to its boundaries. This is more than true in the field of medical librarianship.

SISTER TERESA LOUISE
Medical Librarian

LIFE INSURANCE IN ESTATE PLANNING TODAY

Is Your Wife the Beneficiary of Your Life Insurance Policies?

Under your present estate plan, you may have named your wife as beneficiary of life insurance proceeds which qualify for the marital deduction, while other assets are to go to your children. But assuming you are willing to give up your rights in the policy, it may now be advisable for estate tax purposes to reverse these dispositions by making the children the insurance beneficiaries and providing for the transfer of other assets to the wife. An irrevocable transfer of the policy to the children, or for their benefit, will remove the proceeds from your estate. And the full benefit of the marital deduction can be secured for other assets passing to the wife. If this is not done, all or part of the marital deduction may be wasted.

Do Life Insurance Policies Provide for Payments to Your Wife, with the Principal Going to Your Children or Others on Her Death?

If you die owning a policy with this settlement option, the entire proceeds will be fully includible in your estate with no reduction by reason of the marital deduction, unless your wife has the power to appropriate the principal, or at least to draw it into her estate. And even where provision of such a power does give the husband's estate the benefit of the marital deduction, any portion of the proceeds not used up by the wife during her life will be included in her estate at her death.

There is a way of satisfactorily providing for both wife and children and avoiding estate tax on the insurance proceeds in both estates—and this can be done without having to use the marital deduction. The insured transfers the policy to his wife irrevocably—taking care that neither the policy nor proceeds can come back to him or his estate. It is also provided that on the insured's death, the income from the proceeds is to be paid to the wife during her life. On her death the principal is to be paid to the insured's children.

Under this arrangement there is no estate tax on the proceeds when the insured dies, assuming the Treasury does not find that he transferred the policy "in contemplation of death." Nor is there any estate tax on the proceeds when the wife dies first—and thus dies owning the policy—the value

of the policy will be included in her estate. Yet even this eventuality may be prevented by having a trustee hold the policy instead of the wife.

Furthermore, estate tax can be entirely avoided or reduced to a nominal sum even though the wife is given (in addition to income) the right to take part of principal during her life. This can be achieved by limiting her right to take principal to an ascertainable standard relating to her health, support, maintenance, etc. Such a right is classed as "nontaxable" and the unspent principal can go to the children free of any tax in the wife's estate.

Are Proceeds of Insurance on Your Life Payable to Your Wife Under the Interest Option?

Under the interest option, payments representing principal would not be taxable income to your wife, but payments representing interest would be fully taxable. Thus it may be to her benefit if the option is changed to give her the proceeds in installments.

That part of each installment which represents principal is tax-exempt. That part of each installment which represents interest (including excess interest dividends) is also exempt up to an amount not exceeding $1,000 a year.

There is no longer any income tax advantage in electing the installment option for beneficiaries other than the wife since any amount they receive in excess of the principal proceeds is fully taxable.

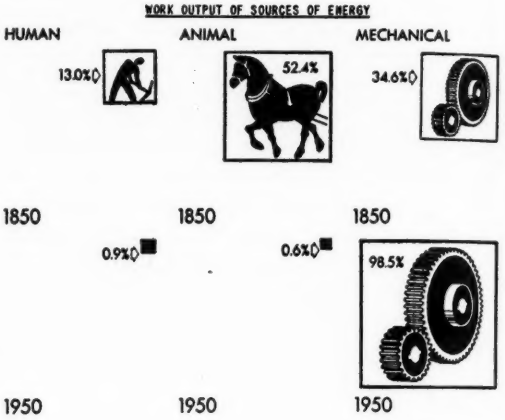
It may be helpful in your planning to know how much insurance payable in installments over the widow's lifetime would yield roughly $1,000 annually in interest so that only a negligible amount need be reported in gross income. There is no precise answer for any given case since it would be necessary to know the wife's age at the time payments begin—which can't be determined until the husband dies. But this can, of course, be estimated and the necessary amount of insurance approximated.

Assuming the husband's death when the wife is fifty-seven, her life expectancy would be twenty-four years. About $63,000 of life insurance would produce an annual payment of $3,636, of which $1,011 would be interest and $2,625 would be principal.

ALAN W. GILES

ECONOMIC HISTORY

The Twentieth Century Fund, a non-profit research organization, has just published a new survey of the past and future potentials of the



American economy. The current study is designed to present in simple language and graphic illustration some of the highlights of a previously published but highly technical treatise on this same subject.

A typical example of the many charts and illustrations in the study is the accompanying one which shows how mechanical power has almost completely supplanted animal and human muscle power since 1850.

This illustration is of particular significance because the study says that it is the increased use of power and machinery to do our work which has been largely responsible in our having the highest standard of living in the world. In this connection the study says:

"Certainly high productivity is the key to the entire achievement. Rising productivity centers around a worker's ability to turn out an increasing amount of goods or services in an average hour's work. The plant, materials and management supplied by the employer, and the energy, skill and spirit of the worker are important in this process.

"But neither the competence of management nor the efforts of the worker supply the most basic reason for the steep upward trend of American productivity. . . . The fabulous increase in our output per man-hour over the past century has been due to the steady expansion of our factories and productive plant and our skill in working out constantly better methods and processes and providing more and better machinery to back up the human worker with vast amounts of inanimate energy. . . .

"There is the central principle of our success, the secret of our phenomenal rise in productivity. We shall encounter the results of this principle many times as we look into every part of our entire economic system to get the full aspect of America's new dimensions."

There have, of course, been many reasons advanced over the years as to why the United States should have found the unique combination to make us the richest nation in the world. We have little more than 6 per cent of the world's population and less than 7 per cent of its land area. Also, we have by no means a monopoly on natural resources. Perhaps, however, the following comments from the original Twentieth Century Fund study will bear reproduction as they offer some very compelling thoughts on this matter:

"The relative 'classlessness' and fluidity of American society, the absence of an aristocratic attitude toward trade as an occupation, together with abundant opportunities for business success, created an atmosphere that attracted into business the gifted and superior youths who in the older countries might have chosen careers in the army, the law, or the ministry. In the United States, to a much greater extent than in other countries, business success was generously rewarded, not only in material terms but in the coin of social approval and public esteem.

"These ideas and attitudes, developing within a 'hybrid population' that was spreading rapidly over a new continent, created a political and social climate favorable to invention and innovation, to the growth of individual enterprise, to the willingness to take risks and invest capital. America's unique industrial achievements are the result not only of favorable climate, soil and resources but to an indeterminable extent of these more subjective factors. A skilled, vigorous population—an individualistic, aggressive people with an extroverted approach toward themselves and their environment—has probably been more crucial to our technical development than the objective factors of climate and resources. In the last analysis, it is the attributes—and the attitudes and ideals—of the American people which account for the dynamic character of the American economic system."

From *Brevits*
By permission of EDWARD E. HALE
Vance Sanders Company

EDUCATION AND STATE GOVERNMENT

Education is not only one of the major responsibilities of state government, but it is also a function of government that is most essential to the progress and happiness, as well as the prosperity and security, of all the people.

Today there are new factors and trends in our society that contribute toward making our problems and responsibilities in the field of education more urgent and more important than ever before. Outstanding among these is the increase in our birth rate, that has placed an unprecented burden of expansion on our schools. The increased numbers of children, born in the early forties and later, have swelled the numbers in our elementary and secondary schools, and the oldest of them are just now about to enter college. Because of the low birth rate in the thirties, our college age population is now at its low point. But in the next few years the tremendous pressure of increasing numbers will reach our institutions of higher education.

Geographical changes in our population, primarily in the phenomenal growth of the suburbs, have made problems of school facilities there particularly acute. Social economic and technological changes in our society require an ever increasing proportion of people with higher education, not only in specialized scientific fields but also in the area of sound, broad, liberal education. And constantly increasing costs of education, together with the increasing cost of other governmental functions, make the problem of finance, and a wise sharing of these costs between local districts and the state, one that needs continuing study and evaluation.

I regard education as of such importance that I sent a special message to the 1957 Minnesota Legislature, making specific and detailed recommendations in this field. We have had the sincere, vigorous, and effective co-operation of the Legislature, of agencies and departments of state government, of school boards and of voluntary organizations of teachers, parents, and citizens. I am happy to report that I believe the progress made in legislation for education in Minnesota was greater at the last legislative session than at any other time in our history.

This progress was especially important in extending various kinds of special education, and in providing increased support both for elementary and secondary schools and for higher education.

We have stepped up our program in vocational rehabilitation so that in 1957 there were 967 rehabilitated as compared with 582 in 1955, and 679 in 1956. This increase is of even greater significance in view of the fact that the number of rehabilitations of persons classed as severely

disabled was more than doubled—from 85 to 181—last year. This achievement, of course, required an increased staff; and we have adopted the policy of making grants to specialized agencies, such as the Rehabilitation Center at the University of Minnesota, to enable them to provide greater services.

Last year likewise marks a major step forward in educational services for exceptional children. A new law provides that every school district must provide special instruction and service for handicapped children of school age, and provides for financial and supervisory assistance for this program. Continued progress and improvement of the state program for children needing special educational will be assured by an act which created an Advisory Board on Handicapped, Gifted and Exceptional Children.

Public schools in Minnesota are supported by local school districts with substantial contributions from the state, plus comparatively small federal contributions, primarily in the field of vocational education. State aid in substantial amounts tends to equalize educational opportunity throughout the state. It also prevents the levying of a heavier tax burden on property—for the property tax is the chief source of revenue for local school districts. If the proportion of school support which comes from the state were increased, the tax load on property could be lightened, and we could carry out still further the principle of equalization. This would, however, mean still further increases in appropriations at the state level.

The people of Minnesota are giving increased attention to their schools. I am sure they recognize not only that education must be paid for, but also that it is something too valuable to be neglected.

ORVILLE L. FREEMAN
Governor of Minnesota

GANGLIONIC AND ADRENERGIC BLOCKING AGENTS

(Continued from Page 251)

11. Folkow, B.: Nervous control of the blood vessels. Physiol. Rev., 35:629, 1955.
12. Green, H. D., Gobel, W. K., Moore, M. J. and Prince, T. C.: An evaluation of the abiltiy of Priscoline, Regitine, and Roniacol to overcome vasospasm in normal man. Circulation, 6:520, 1952.
13. Green, H. D.: Comparison in man of adrenergic blockade produced by Dibenzyline, Ilidar, Priscoline, and Regitine. Circulation, 15:47, 1957.
14. Green, H. D. and DuBose, H. H.: Clinical trial of Ilidar, a new dibenzazepine adrenergic blocking drug, in the treatment of peripheral vascular diseases and miscellaneous complaints. Circulation, 10:374, 1954.
15. Green, H. D. and Grimsley, W. T.: Effects of Regitine (C-7337) in patients, particularly those with peripheral arterial vascular disease. Circulation, 7:487, 1953.
16. Green, H. D.: Pharmacology of Antihypertensive Drugs. Am. J. Med., 17:70, 1954.
17. Green, H. D.: Adrenergic blocking drugs, 28/1-28/17. In: Drill, Victor A. (ed.): Pharmacology in Medicine. New York: McGraw-Hill, 1954.
18. Green, H. D.: Exhibit—Pharmacology of Antihypertensive Drugs. p. 129. Abstracts of the Eight Annual Scientific Assembly, American Academy of General Practice, Washington, D. C., March 19-22, 1956.

FUNDAMENTALS OF ANTICOAGULANT THERAPY

(Continued from Page 255)

or peripheral arterial embolism, it is usually advisable to start treatment with heparin and a coumarin anticoagulant and to continue use of the coumarin agent as soon as its effect has reached the therapeutic range, the use of heparin then being discontinued. However, heparinization at the beginning of anticoagulant therapy usually is not employed after acute myocardial infarction.

Summary

The use of anticoagulants is a valuable therapeutic adjunct. It requires careful supervision, some experience on the part of the physician and close attention to the establishment and maintenance of adequate degrees of anticoagulant effect within the prescribed therapeutic range. For such supervision when one of the coumarin compounds is used, there is no substitute for the one-stage measurement of prothrombin time, which must be done at sufficiently frequent intervals to insure that an adequate but not excessive effect is being maintained. A small risk of bleeding is always present when anticoagulants are used, and this must be calculated in determining the advisability of such treatment for any individual patient. However, the threat to life by such bleeding is usually much less than the threat to life by the thrombosing disorder for which the treatment is considered.

President's Letter

A MOST REWARDING COMMITTEE—PHYSICIAN'S ASSISTANCE

To its members, the Physicians' Assistance Committee is the most satisfying committee of the State Medical Association. These men rarely miss a meeting, although they travel from the four corners of the State, and they return to their homes with interest and zeal renewed.

Visualize the situations that bring members of the committee together. The elderly doctor has for years taken care of the community. He has been its comforter in trouble, its first source of help in sickness, its aid in the presence of accident. He may have been an outstanding citizen, a pillar of the Church, a sparkplug for its youth program, the backer for school athletics, and always the guardian of the public health. He almost surely has helped many of the individual members of the community over hard spots, both physical and financial, and has often omitted sending his bills, or has actually spent his money to help the poor. As he grows old, he cannot work as hard, may have a stroke or break a leg, may even lose his memory, or his carefully planned investments may go sour. By this time, those old bills are uncollectable, but his expenses continue, and may increase.

The physician is proudly individual. He is reluctant to accept help from another individual, nor does he wish to be a public charge. He does not like the idea of a compulsory social security. Who, then, but his fellow physician can come to his aid? The Physicians' Assistance Committee was set up for just this function, assistance by his own profession to the physician in trouble.

The members of this committee have worked in a dedicated manner. The committee was appointed in 1953. Dr. E. R. Sather of Alexandria, Dr. E. A. Kilbride of Worthington, and Dr. Herman Juergens of Belle Plaine were Charter members and have not missed a single meeting in almost five years. Dr. James Blake of Hopkins, Dr. Paul Boman of Duluth, Dr. John Dordal of Sacred Heart and Dr. W. E. Macklin of Willmar have missed only one meeting in all that time. Such devotion is hard to find, and comes only from dedicated men who are convinced of the value of the cause. The project was the idea of Dr. W. R. Humphrey of Stillwater, who has been chairman until now. Dr. Humphrey himself has been forced to give up his activities because of ill health. His committee chairmanship has been taken over by Dr. James Blake who carries on with his usual thoroughness and enthusiasm.

It is, indeed, warranted that credit be given to these men who give so freely of their one completely irreplaceable resource—their time.

Horatio B. Sweetser

President, Minnesota State Medical Association

Medical Economics

Edited by the
Committee on Medical Economics,
Minnesota State Medical Association
George Earl, M.D., Chairman

MINNEAPOLIS TOPS U.S. ON MEDICAL CARE COSTS

Minneapolis is the highest priced city in matters for consumer costs for medical care. This disclosure was made recently in the monthly report of the Bureau of Labor Statistics.

For food, clothing, transportation and all other essential items combined, cost of living is higher in Boston, Chicago, Detroit, Portland and Los Angeles. But for medical care alone, Minneapolis' index of 171.6 is the nation's highest. Or at least it was at the end of January. This compares with the national average of 141.7, which represents a 0.6 per cent rise over the previous month.

The increase, said the Labor Department, "resulted from scattered reports of advances in fees for professional services and hospital rates. Group hospitalization insurance premiums also rose in a few cities."

RETAIL DRUGGISTS TESTIFY ON BEHALF OF JENKINS-KEOGH BILL

George H. Frates, Washington representative of the National Association of Retail Druggists in testimony given before the House Ways and Means Committee, urged passage of the Jenkins-Keogh bill to "correct a discrimination that has unfairly penalized those who work for themselves rather than for others." He declared:

"Why should a corporation or an individual conducting some other form of a business who hires people, be permitted to defer a portion of taxable income from taxation by setting it up in a retirement fund, when the small, independent, retail pharmacist cannot do likewise? We have been told many, many times by the honorable members of Congress that small business is the backbone of the nation. If this be true, the Congress should overwhelmingly enact H.R. 9 and H.R. 10 into the law. These are days of challenge for small business—for the small self-employed person. . . . This proposed legislation would permit the individual operator to deduct from his total income a fixed percentage or dollar amount on which he would pay no income tax. He would be allowed to invest this money in a pension retirement fund. Only when he used this fund in later years would he pay income taxes on the money."

MEDICARE ISSUES RULES ON DRUGS AND ID CARDS

Medicare headquarters has continued authorizing of drugs to maternity patients by civilian physicians. ODMC Letter No. 9-58 makes this clear to dispel confusion or uncertainty in this regard rising out of earlier directives. To receive reimbursement for drugs supplied to maternity patients, either directly or through pharmacy channels, the physician should itemize the drugs and their cost on the claim form (DA Form 1863) or on an attachment thereto. Nomenclature, quantity and cost of the medicinals must be shown.

Many servicemen's dependents are presenting themselves for Medicare hospital and medical benefits without their official identification cards. ODMC Letter No. 10-58 points out that the doctor or hospital should call for one of the following, if the prospective patient cannot produce the regular card (DD Form 1173):

Statement of the local commander that the patient is eligible dependent. Official documents or identification cards, other than DD 1173, attesting to eligibility for civilian services under Medicare.

Statement by physician or hospital authority that he has personal knowledge of the patient, dependency status and eligibility for Medicare.

ODMC Letter No. 9-58 also deals with Medicare coverage of eligible dependents under age twenty-three who are in full-time study in institutions of higher learning. Such institutions must be listed in "Education Directory 1955-56, Part 3, Higher Education." This guide is purchasable ($0.50) from Supt. of Documents, Washington 25, D. C.

AGED LACK HEALTH INSURANCE

Only one-third of the nation's population over the age of 65 have any form of health insurance protection. This is one of the facts brought out as the result of a recent survey made by the New York State Joint Committee on Aging.

The survey points out that because of their high incidence of disease and disability, insurance com-

panies are reluctant to underwrite medical expense for this age group, according to the Commission, and as a result, sickness too often brings medical indigency.

Currently, most companies will not provide coverage for the aged, and if they do, the premiums are considerably higher. One solution suggested has been a small premium increase for all age groups amounting to about 3 dollars per persons annually to absorb the additional cost of covering the aged; however commercial health insurance carriers maintain that competition will not permit increasing the premiums for younger policyholders, and many keep premium costs down by canceling individual policies at ages sixty-five, seventy or seventy-five. Others do not permit group policies, which comprise the largest proportion of health insurance, to be converted to individual contracts at retirement.

However, there are indications that the picture is growing brighter. Some private carriers are experimenting with covering for specialized groups of older people; for example, a company in Chicago recently wrote a group hospital-surgical contract covering more than 23,000 members of the National Association of Retired Employees.

The Health Insurance Institute reports 1957 saw expansion of health insurance to include protection for more and more of the population. Policies designed to afford coverage for retired workers and for those over sixty-five continued to increase in number. A recent nationwide survey indicated that the number of group insurance plans offering the retired worker the option to either continue his insurance under the group or to convert his health insurance coverage to an individual policy has more than doubled within the last four years alone. Recently introduced commercial health insurance plans with paid-up premiums at age sixty-five are also becoming increasingly popular, the Institute found, while significant advances were noted in the number of policies in force which guarantee renewal by the insurance company.

DISCIPLINARY ACT UPHELD BY COURT

The Supreme Court of Washington has affirmed the action of the disciplinary board operating under the Washington medical disciplinary act.

The board had suspended the license of a physician who was convicted of violating the internal revenue code by filing a false and fraudulent income tax return. This is believed to be the first case to have come before the Supreme Court of Washington under the medical disciplinary act which was adopted in 1955.

AMA NEWSPAPER TO MAKE DEBUT

The AMA News, a sixteen-page tabloid newspaper, will be introduced at the AMA annual convention in San Francisco, June 23-27.

The new publication will be distributed every two weeks to approximately 200,000 physicians.

Purpose of the new publication will be to bring to the attention of AMA members the multitide of projects and activities carried on by the association, as well as all non-scientific news of interest to the profession. Publishing a newspaper for members was selected as a means of improving communications between the association and its members.

Physicians will be kept informed of what is going on in medicine in all 48 states through *The AMA News*.

AMA GROWS

AMA membership of all classifications, as of September 30, 1957, rose to a record total of 168,399 members in all classifications. Included were 145,452 active members, 6,057 associate members, 16,512 service members, 289 affiliate members, and 89 honorary members.

NATIONAL JAYCEES HEALTH PROGRAM

More than 3,000 local chapters throughout the nation are participating in year-round health programs. Ten suggested activities have been planned including Salk Vaccine Campaign; Health Fair; Better Sight and Hearing for Children; Poison Control; Assistance to Mental Health for Youth; Adventures in Living for Older People; Help for Handicapped Children; Recreation for Mental Patients; Jaycee Health Forums; and Directory of Health Services.

U.S. MEDICAL POST IN DOUBT

A house bill introduced by Reps. Carl Vinson (D., Ga.), Leslie C. Arends (R., Ill.) and Paul Kilday (D., Texas), would kill the post of Assistant Secretary of Defense for Health and Medical Affairs. Dr. Frank B. Berry now holds the post created at the time of the Korean hostilities.

ARTHRITIS CAPSULES CURBED

A consent order restricting advertising claims for "Warsene Capsules" as a treatment for arthritis and rheumatism has been approved by the Federal Trades Commission. The order names a St. Louis firm and its former officers.

FDA CRACKS DOWN ON QUACKS

Six dubious therapeutic devices have been reported seized by the Food and Drug Administration in the month of January. Included were two taken from the office of a physician-chiropractor and used for cancer, congestion, etc.; another removed from a chiropractor's clinic because of peculiar labeling; and three seizures were made from a commercial firm whose representations were challenged by FDA.

UNITED STATES—RUSSIAN MEDICAL SCIENTIST EXCHANGE PLAN

A two-year period of multiple exchange programs of medical scientists has been agreed upon by the United States and Russia. Three or four medical scientists will be sent to the United States this year by the Russian Ministry of Health to deliver lectures and exchange experiences during a two or three week period. A similar group from this country will go to Russia.

BARBITURATE REFILLS QUESTIONED

Narcotics Commissioner, H. J. Anslinger, testifying before a House Appropriations sub-committee, has again questioned the advisability of issuing refills for barbiturate prescriptions. He told of one woman who was allowed to have a seconal prescription refilled 300 times "winding up, of course, in the insane hospital. . . . I do not think they should be allowed to be phoned in . . . that should not be." He said, however, that tranquilizers appear to have no attraction for narcotics addicts. "That is always a good sign, because when you see a drug addict interested in some new form of medication, some new synthetic drug, that is the one to watch. He is not interested in the tranquilizers."

FOURTEEN REASONS WHY THE FORAND BILL SHOULD NOT BE PASSED

The Medical Society of the State of Pennsylvania in the March *Newsletter* listed the following fourteen reasons why the Forand Bill should not be passed. They are:

1. It would destroy a significant area of voluntary health insurance coverage. The establishment of a compulsory federal system of providing hospital and surgical services for those eligible for social security benefits would terminate voluntary health insurance experimentation for the aged and result in the cancellation of a large number of policies. The aged would have no incentive to provide private health insurance coverage for themselves (approximately 50 per cent are now covered). Those now covered offer proof of the financial ability and willingness of a large segment of the aged population to acquire medical care without government interference.

2. Hospital and surgical services for the older population can be handled by community and voluntary means. In 1950, only 20 per cent of those over age sixty-five were covered by voluntary health insurance. Approximately 50 per cent now have some coverage. Assuming this expansion continues, within a few years virtually all of the insurable oldsters will be enrolled.

3. It would mean another assault on the pocketbook of the taxpayer. This plan would result by 1957 in an increase in federal OASI taxes of up to $213.00 annually ($106.50 for the employe and $106.50 for the employer.) This 59 per cent increase would result in annual payments of $285.00 for each by 1957. The tax for self-employed persons would be $427.50 annually. Proposed income tax reductions would be more than offset by these social security tax increases.

4. A large percentage of beneficiaries under the bill do not need assistance. All eligible social security retirement and survivor recipients, even though they are gainfully employed or able to pay for hospitalization and medical care, would receive benefits under the bill.

5. It would immediately nationalize a large segment of hospitalization and medical care. The federal government would control standards of hospital and surgical services and the conditions under which services are provided.

6. It limits free choice of hospitals and physicians. Only those hospitals and doctors entering into contracts with the federal government could participate in the program. Participation by hospitals and physicians could be arbitrarily restricted for administrative reasons.

7. The personal relationship between the doctor and his patient would be jeopardized. Government regulations would be imposed on patient and physician alike, bringing a third party into the relationship.

8. It would violate the basic concepts of the social security program. Since its inception, social security has provided benefits in terms of dollars which many people have used as a floor in planning their retirement needs. The interjection of the service benefit concept into the law (Which the Forand bill does for the first

time) would alter the basic program and would cause a financial drain that could wreck the retirement program. In fact, under the existing program, this year, for the first time, the system will receive less income than it will pay out in benefits.

9. It would stimulate over-utilization of hospital and medical services. In many countries where similar legislation is in effect, there has been a staggering increase in use of hospital facilities by those over sixty-five. (In Saskatchewan, Canada, the average person over sixty-five occupies a hospital bed 7.2 days a year; in the United States the average person over sixty-five occupies a hospital bed 2.5 days a year.) Over-utilization of hospitals would limit the number of beds available for the acutely ill of all ages in the community.

10. Community incentive to support voluntary hospitals would be virtually eliminated. Local communities would shift the responsibility for building and operating hospital facilities to the federal government.

11. The government would assume the role of price and wage fixer. Under the Forand proposal, the federal government would be given the right to fix the fees and charges to be paid to the participating physicians and hospitals. Historically, when such a principle as this is once established, it is extended to other segments of the population. The fixing of fees and charges by government would be a step toward a controlled and regimented economy.

12. Many aged persons would become unduly concerned with their health. By eliminating personal financial responsibility, many aged persons would seek unnecessary hospital and medical care for trivial and imaginary illnesses.

13. It would discourage family responsibility. Most families assist in caring for their aged members. The Forand bill would tend to destroy this traditional family responsibility and moral concept.

14. Other age groups would demand the same benefits. Soon the program would be extended to the entire population. This development would completely nationalize our hospitals and the practice of medicine.

SPICY SUGGESTIONS

Good news for patients on sodium-free diets—more than thirty different spices and other foods have been found to brighten the flat taste of salt-free foods and make them palatable. Suggested condiments include: Angostura Aromatic Bitters (used primarily in the preparation of alcoholic drinks), allspice, almond extract, basil, bay leaves, cardamon, carroway, chili powder, cinnamon, clove oil, cocoanut, curry, dill, garlic, ginger, honey, homemade horseradish, jams, lemon juice, lime juice, mace, marjoram, mushrooms, mustard seed, nutmeg, onion, paprika, parsley, freshly ground pepper, peppermint, pimiento, rosemary, saffron, savory, sesame, sugar, tarragon, thyme, vanilla and vinegar.—*American Journal of Nursing*, February, 1958.

LOCAL EDEMA OF LOWER EXTREMITIES

(Continued from Page 259)

Summary

The differentiation of edema with regard to local or systemic causes, the relative benignity of swelling of the lower extremity resulting from local causes and the reassurance of the patient that such edema is benign are important considerations. Proper and continuing treatment, especially of chronic venous insufficiency and lymphedema, although difficult, is necessary in order to prevent the complications and invalidism that are sequelae of improper treatment.

SURGICAL TREATMENT OF AORTIC INSUFFICIENCY

(Continued from Page 262)

8. Taylor, W. J., Hoover, W. B., Black, H., Harkens, D. E.: The surgical correction of aortic insufficiency. J. Thoracic Surg. (in press).
9. Wible, J. H., Jacobson, L. F., Jordan, P., Jr., Johnston, C. G.: The correction of aortic insufficiency with a spring valve prosthesis. A.M.A. Arch. Surg., 74:929 (June) 1957.
10. Roe, B. B., Najarian, J. S., Moore, D.: A technic for insertion of a flexible aortic valve prosthesis into the ascending aorta. Ann. Surg., 145:388, 1957.
11. Malette, W. G., Summers, W. B., Eiseman, B.: Experiment problems in construction of subcoronary prosthetic aortic valves. (Am. Coll. Surg.) Surg. Forum (1956), 7:233, 1957.
12. Gould, S. E.: Pathology of the Heart. Springfield, Illinois: Charles C Thomas, 1953.
13. Alai, J., Adam, A., Veri, F., Jamison, W. L.: Production of aortic insufficiency with a study of arterial tracings. Surgery, 36:237, 1954.
14. DeWall, R. A., Warden, H. E., Varco, R. L., Lillehei, C. W.: The helix reservoir pump-oxygenator. Surg. Gynec. & Obst., 104:699, 1957.
15. Melrose, D. G., Dreyer, B., Bertell, H. H., Boher, J. B. E.: Elective cardiac arrest. Lancet, 269:21, 1955.
16. Wiggers, C. J.: The arterial pulse. Circulation in Health and Disease. Philadelphia: Lea and Febiger, 1923.
17. White, P. D.: Heart Disease. New York: MacMillan, 1956.
18. Wood, P.: Diseases of the Heart and Circulation (2d ed.). Philadelphia: J. B. Lippincott Co., 1956.
19. Wilder, R. J., Moscovitz, H. L., Ravitch, M. M.: Aortic insufficiency. J. Thoracic Surg., 33:147, 1957.
20. Garamella, J. J., Oropeza, R., and Andersen, J. G.: The surgical treatment of aortic insufficiency by open plastic revision of the tricuspid aortic valve to a bicuspid valve. Surg. Gynec. & Obst. (in press).

Minnesota State Medical Association

105th Annual Meeting

Minneapolis, Minnesota—May 22-24, 1958

BUSINESS SESSIONS

Hotel Leamington

TUESDAY, MAY 20

2:00 P.M.—Council
Dubonnet Room, Hotel Leamington
6:00 P.M.—Council Dinner
8:00 P.M.—Council
Dubonnet Room, Hotel Leamington

WEDNESDAY, MAY 21

8:30 A.M.—Council
Dubonnet Room, Hotel Leamington
10:00 A.M.—Reference Committees
Rooms to be assigned
2:00 P.M.—House of Delegates
Hall of States, Hotel Leamington
6:00 P.M.—New Members and County Officers Dinner
Town Hall, Hotel Leamington
8:00 P.M.—House of Delegates
Hall of States, Hotel Leamington

THURSDAY, MAY 22

8:00 A.M.—Committee Breakfasts
Rooms to be assigned
8:30 A.M.—Council
Dubonnet Room, Hotel Leamington
12:15 P.M.—House of Delegates
Hall of States, Hotel Leamington

FRIDAY, MAY 23

8:00 A.M.—Committee Breakfasts
Rooms to be assigned
8:30 A.M.—Council
Dubonnet Room, Hotel Leamington

SATURDAY, MAY 24

8:30 A.M.—Council
Dubonnet Room, Hotel Leamington

SOCIAL EVENTS

WEDNESDAY, MAY 21

Dinners

New Members and County Officers Dinner
6:00 p.m. Town Hall, Hotel Leamington

Golf Dinner
6:30 p.m. Edina Country Club

THURSDAY, MAY 22

Luncheon

Medical Women's Association
12:00 noon. Normandy Hotel, 405 South 8th St., Minneapolis. All women physicians are invited to attend the luncheon sponsored by Alpha Epsilon Iota Medical Sorority. Come and get acquainted and enjoy an interesting program. Dr. Harriet Blodgett, Director of Sheltering Arms School, will speak on "What Happens to the Retarded Child When He Leaves the Doctor's Office." Luncheon tickets are $2.50. Reservations must be made before May 15. Send checks to: Dr. Helen Dahl, 4708 Isabel Ave., Minneapolis, phone number PArkway 4-0179.

Dinners

Minnesota Academy of General Practice
6:00 p.m. Town Hall, Hotel Leamington. Tickets, $5.00, gratuity included. Speaker: Harry F. Dowling, Professor of Medicine and Department Head, University of Illinois College of Medicine, Chicago. His topic will be "The Doctor as a Teacher."

Minnesota Academy of Ophthalmology and Otolaryngology
6:00 p.m. Minnesota Club, St. Paul. Marshall M. Parks will speak on "The Importance of Early Strabismus Care."

Minnesota Radiological Society
7:00 p.m. Gold Room, Radisson Hotel. Tickets may be purchased at the dinner.

Minnesota State Medical Association
9:00 p.m. OPEN HOUSE, Hall of States, Hotel Leamington. All physicians and their wives are invited to attend the annual entertaining OPEN HOUSE variety program as guests of the Hennepin County Medical Society.

FRIDAY, MAY 23

Luncheon

12:15 p.m. *Minnesota Society of Clinical Pathologists.*

Dinners

Minnesota Society of Clinical Pathologists
6:00 p.m. Annual Dinner and Business Meeting, Curtis Hotel.

Annual Banquet, Minnesota State Medical Association
7:00 p.m. Hall of States, Hotel Leamington. Tickets are $5.00, gratuity included.

Speaker: David B. Allman, President, American Medical Association.

Introduction of Woman's Auxiliary President: Mrs. Reuben Erickson, Minneapolis.

Presentations:
Fifty Club Certificates
Southern Minnesota Medical Association Medal
Distinguished Service Medal

ROUND TABLES

Hotel Leamington—12:15 P.M.

THURSDAY, MAY 22

Office Gynecology.....JAMES S. HUNTER, Rochester
Hemorrhage in Obstetrics
GRANT F. HARTNAGEL, Red Wing
Abuse of Steroids.....CHARLES H. SLOCUMB, Rochester
How to Handle Drug Addiction
E. M. HAMMES, JR., St. Paul
Psychiatric Aspects of Obesity
JOHN E. T. HAAVIK, Duluth
Causes of Gastro-Intestinal Hemorrhage
M. H. STAUFFER, Rochester
The Sexual Deviate....BERNARD C. GLUECK, Minneapolis
Uses of Radioisotopes.....ELMER PAULSON,
JOSEPH RYAN, St. Paul

FRIDAY, MAY 23

Office Dermatology ....ROBERT R. KIERLAND, Rochester
Drug Therapy in Hypertension
JAMES J. COLL, Duluth
Treatment of Post-operative Shock
ELLIS N. COHEN, Minneapolis
Office Proctology..CHARLES A. NEUMEISTER, Minneapolis
Fractures in the Upper Extremities of Children
D. L. MCCAIN, St. Paul
Newer Insulins.....MOSES BARRON, Minneapolis
The Obstetrician's Role in Perinatal Mortality
JOHN S. GILLAM, Fargo, North Dakota

GENERAL SESSION

Minneapolis Auditorium

THURSDAY, MAY 22

Morning Session

Chairman: J. P. MEDELMAN

A.M.
8:30 Visit Scientific and Technical Exhibits
9:00 EMERGENCIES—Panel Discussion—
Moderator, JOHN E. TWOMEY, Minneapolis
Poisoning.....ROBERT D. SEMSCH, Minneapoilis
Medical Cardiac Emergencies
RICHARD J. FREY, Minneapolis
Unconscious States..H. F. R. PLASS, Minneapolis
Catastrophic Drug Reactions
L. E. PRICKMAN, Rochester

10:15 INTERMISSION
Visit Scientific and Technical Exhibits

11:00 RUSSELL D. CARMAN MEMORIAL LECTURE
Radiation Hazards in Clinical Medicine
RICHARD H. CHAMBERLAIN, Professor of Radiology, University of Pennsylvania School of Medicine and Graduate School of Medicine, Philadelphia, Pennsylvania

Discussion
JAMES MARVIN, PH.D., University of Minnesota
DONN G. MOSSER, University of Minnesota

Afternoon Session

Chairman: WM. D. COVENTRY

P.M.
12:15 Round Table Luncheons
1:30 Visit Scientific and Technical Exhibits
2:00 THE FAMILY DOCTOR'S RESPONSIBILITY TO HIS PR-SCHOOL EYE PATIENT
Moderator—W. J. BUSHARD, Minneapolis
Amblyopia .....THEODORE MARTENS, Rochester
Visual Acuity.....WALTER FINK, Minneapolis
Recognition of Strabismus
JOHN MCNEILL, Saint Paul
Diagnosis and Management of Other Eye Problems
MARSHALL PARKS, Clinical Instructor of Ophthalmology, Georgetown University, Washington, D. C.
Tracheotomy: When, Why and How
ROBERT E. PRIEST, Minneapolis

3:15 INTERMISSION
Visit Scientific and Technical Exhibits

3:15 Obstetric Manikin Demonstration
GRANT F. HARTNAGEL, Red Wing
4:00 WHAT'S NEW IN DERMATOLOGY—Panel Discussion — Moderator, FRANCIS LYNCH, Saint Paul
Treatment of Superficial Mycoses
HAROLD G. RAVITS, Saint Paul
Treatment of Acne
FREDERICK T. BECKER, Duluth
Eczema of the Hands
CARL W. LAYMON, Minneapolis
Use of Sedatives and Tranquilizers
ROBERT R. KIERLAND, Rochester
5:15 Visit Scientific and Technical Exhibits
6:00 Special Dinners
9:00 Open House....Hall of States, Hotel Leamington

GENERAL SESSION

Minneapolis Auditorium

FRIDAY, MAY 23

Morning Session

Chairman: J. E. TWOMEY

A.M.
8:30 Visit Scientific and Technical Exhibits
9:00 SURGERY—Panel Discussion
Micrococcus Infections in the Hospital—1958
WESLEY W. SPINK, Minneapolis
Fluid Balance and the Acutely Injured Patient
BERNARD ZIMMERMANN, Minneapolis
Management of Head Injuries
WALLACE RITCHIE, Saint Paul
Inguinal and Femoral Hernioplasty
CHESTER B. MCVAY, Clinical Professor of Surgery, University of South Dakota Medical School, Yankton, South Dakota

10:15 INTERMISSION
Visit Scientific and Technical Exhibits

11:00 MINNESOTA DIVISION, AMERICAN CANCER SOCIETY LECTURE
The Cell as a Mirror of Disease
JAMES W. REAGAN, Associate Professor of Pathology and Director, Laboratory of Cancer Research, Western Reserve University, Cleveland, Ohio

11:30 ARTHUR H. SANFORD LECTURE IN CLINICAL PATHOLOGY
The Spontaneous Regression of Cancer
WILLIAM BOYD, Emeritus Professor of Pathology, University of Toronto, Toronto, Ontario

Afternoon Session

Chairman: R. N. BARR

P.M.

12:15 Round Table Luncheons

1:30 Visit Scientific and Technical Exhibits

2:00 VIRUSES AND VIRUS DISEASES—Panel Discussion

Moderator—GAYLORD ANDERSON, University of Minnesota

Current Virus Disease Problems in Minnesota
HERMAN KLEINMAN, University of Minnesota

NORTHWESTERN PEDIATRIC SOCIETY LECTURE

Immunization With Orally Administered Attenuated Live-Virus Poliomyelitis Vaccine
MAURICO M. DA SILVA, Communicable Diseases Branch, Pan American Sanitary Bureau, Washington, D. C.

Some International Aspects of Virus Diseases
FRED L. SOPER, Director, Pan American Sanitary Bureau, Washington, D. C.

3:15 INTERMISSION
Visit Scientific and Technical Exhibits

3:15 Obstetric Manikin Demonstration
JOHN S. GILLAM, Clinical Instructor, Obstetrics and Gynecology, University of Minnesota, Fargo, North Dakota

4:00 WORLD HEALTH ORGANIZATION STUDIES AND REPORTS

Presiding Officer—WALTER JUDD, Washington, D. C.

Welcome to World Health Organization
CHARLES W. MAYO, Rochester

Address—MARCOLINO G. CANDAU, Director-General, World Health Organization, Geneva, Switzerland

Discussion—LEROY E. BURNEY, Surgeon General, U. S. Public Health Service, Department of Health, Education, and Welfare, Washington, D. C.

5:15 Visit Scientific and Technical Exhibits

6:00 Special Dinner and Meeting

7:00 Annual Banquet
Hall of States, Hotel Leamington

Presiding—O. L. N. NELSON, Minneapolis

Introduction of Woman's Auxiliary President: MRS. REUBEN ERICKSON, Minneapolis

Presentation: Fifty Club Certificates; Southern Minnesota Medical Association Medal; Distinguished Service Award

Address: H. B. SWEETSER, President, Minnesota State Medical Association

Address: DAVID B. ALLMAN, President, American Medical Association, Atlantic City, New Jersey

GENERAL SESSION

Minneapolis Auditorium

SATURDAY, MAY 24

Morning Session

Chairman: W. S. NEFF

A.M.

8:30 Visit Scientific and Technical Exhibits

9:00 MENTAL HEALTH—Panel Discussion—Moderator, WILLIAM C. MENNINGER, Topeka, Kansas

The Thorny Youngster
H. S. LIPPMAN, St. Paul

The Querulous Primigravida
OWEN F. ROBBINS, Minneapolis

The Confused Senior Citizen
J. T. PEWTERS, Minneapolis

Physicians' Feelings
WILLIAM C. MENNINGER, President, The Menninger Foundation, Topeka, Kansas

10:15 INTERMISSION
Visit Scientific and Technical Exhibits

11:00 MEDICO-LEGAL ASPECTS OF HEART DISEASE—Panel Discussion

Moderator—JUDGE WARREN E. BURGER, United States Court of Appeals, Washington, D. C.

MR. ROBERT FARICY, Referee, Minnesota Industrial Commission, St. Paul

HARRY E. UNDERLEIDER, Director, Medical Research, Equitable Life Assurance Society, New York, N. Y.

SIMON DACK, Assistant Clinical Professor of Medicine, New York Medical College, New York, N. Y.

R. W. KISSANE, Professor of Medicine in Cardiology, Ohio State University, College of Medicine, Columbus, Ohio

Woman's Auxiliary

36th Annual Meeting

PROGRAM

THURSDAY, MAY 22, 1958

A.M.

8:30 Registration.....Curtis Hotel

9:45 Executive Board Meeting and Luncheon.... The Woman's Club
Luncheon at 12:15 P.M. Tickets $2.50

P.M.

2:30 Hennepin County Historical Society Tour 2303 Third Avenue S.
Transportation provided. Cars leaving Curtis Hotel for Tour and Tea promptly at 2:15 P.M. and 2:45 P.M.

3:00 Tea.....Minneapolis Art Institute, Fireside Room
All visiting women are cordially invited to be guests of the Woman's Auxiliary to the Hennepin County Medical Society

FRIDAY, MAY 23, 1958

A.M.

8:30 Registration.....Curtis Hotel

9:30 Annual Meeting.....East Room, Curtis Hotel
Open to *ALL* members of the Auxiliary

Presiding—Mrs. C. L. Oppegaard, Crookston, President

Pledge of Allegiance and Auxiliary Pledge—Mrs. F. W. Behmler, Morris
"I pledge my loyalty and devotion to the Woman's Auxiliary to the American Medical Association. I will support its activities, protect its reputation and ever sustain its high ideals."

Address of Welcome—Mrs. Karl W. Anderson, Excelsior, President, Auxiliary to the Hennepin County Medical Society

Response—Mrs. D. E. Stewart, Crookston

Presentation of Convention Chairmen—Mrs. Conrad Holmberg and Mrs. Mancel Mitchell

In Memoriam Service—Mrs. Howard Satterlee, Lewiston

Reports

Election of Officers

P.M.

1:00 Annual Luncheon....Cardinal Room, Curtis Hotel
Tickets $2.50

Installation of Officers—Mrs. H. W. Quist, Minneapolis

Installation of President and Presentation of President's Pin—Mrs. L. P. Howell, Rochester

Presentation of Gavel

Greetings from the New President—Mrs. Reuben Erickson, Minneapolis

3:30 Post-Convention Board Meeting

7:00 Annual Banquet.....Hall of States, Hotel Leamington

Presiding—O. L. N. Nelson, Minneapolis

Introduction of Woman's Auxiliary President: Mrs. Reuben Erickson, Minneapolis

Presentation: Fifty Club Certificates; Southern Minnesota Medical Association Medal; Distinguished Service Award

Address: David B. Allman, President, American Medical Association, Atlantic City, New Jersey

Committees

General Arrangements—Mrs. Conrad J. Holmberg and Mrs. Mancel T. Mitchell.

Reservations—Mrs. Harry B. Hall, Mrs. Roland F. Neumann, Jr.

Tickets—Mrs. James G. Myhre, Chairman; Mrs. D. Keith Millett, Mrs. Wm. E. Petersen, Mrs. O. J. Baggenstoss, Mrs. John W. Johnson, Mrs. John K. Grotting, Mrs. George H. Marking.

Registration—Mrs. Arthur C. Kerkhof, Chairman; Mrs. Harold F. Buchstein, Co-Chairman; Mrs. U. S. Anderson, Mrs. Henry W. Quist, Jr., Mrs. Robert E. Nord, Mrs. Harold E. Miller, Mrs. Dale H. Correa, Mrs. Howard A. Shaw, Mrs. D. M. Thysell, Mrs. Lloyd S. Nelson, Mrs. Nathaniel H. Lufkin, Mrs. Emerson E. Hoppes.

Hospitality—Mrs. Virgil J. Schwartz, Chairman; Mrs. James A. Johnson, Co-Chairman; Mrs. Lester W. Carlander, Jr., Mrs. Hewitt B. Hannah, Mrs. Walter K. Haven, Mrs. Sheldon M. Lagaard, Mrs. Sam Leonard, Mrs. Malvin J. Nydahl, Mrs. Peter J. Schultz, Mrs. Theodore S. Smith, Mrs. Thomas Wright, Mrs. Ferdinand A. Zinter.

Transportation and Tour—Mrs. Conrad I. Karleen, Chairman; Mrs. Elmer T. Ceder, Mrs. Clarence E. Arlander, Mrs. Harold T. Gustason, Mrs. Louis A. Fried.

Press—Mrs. Harold S. Ulvestad.

Flowers—Mrs. Robert G. Tinkham, Chairman; Mrs. Virgil Lundquist, Mrs. Ames W. Naslund.

Pages—Mrs. A. Cabot Wohlrabe, Chairman; Mrs. Willis M. Duryea, Jr., Mrs. William H. Card, Mrs. Kenath H. Sponsel, Mrs. Robert O. Quello.

Executive Board Meeting and Luncheon—Mrs. Robert E. Priest and Mrs. Edward T. Evans.

Tea—Mrs. Edgar A. Webb, Chairman; Mrs. John W. MacDonald, Mrs. Rolf M. Iverson, Mrs. Maynard C. Nelson, Mrs. Howard M. Frykman, Mrs. John P. Wendland.

Annual Meeting and Luncheon—Mrs. James F. Shandorf, Chairman; Mrs. Horatio B. Sweetser, Mrs. Earl T. Opstad.

Music—Mrs. Russell C. Lindgren.

History of Medicine in Minnesota

A MEDICAL HISTORY OF MEEKER COUNTY TO 1900

HAROLD E. WILMOT, M.D.

Litchfield, Minnesota

One hundred years ago the first permanent white settlers arrived in our county. The early history of Minnesota includes Meeker County as part of the Wisconsin Territory. This comprised an indefinite mass of land which was west of the Mississippi, south of the 49th parallel and on westward to the Missouri. Captain Zebulon Pike had assisted in the permanent arrangements for Fort Snelling, and the settlement of Pig's Eye was now overflowing to the steeper banks of the Mississippi on the north and west, to be known in the future as St. Paul. St. Anthony (Minneapolis) was a growing community, and the Indians were steadily being pushed westward.

The area for some sixty miles due west was known as the Big Woods, and to traverse it was an undertaking fraught with perils to quail most of the adventurous spirits of that time. However, the economic pressures in the eastern United States, plus the glowing accounts to induce immigration from Europe, plus the curative benefits of the climate, and the desire to "get rich quick" did produce the characters who became the original settlers of Meeker County.

Meeker County, due in large part to its geographic location, has always occupied a unique niche in the history of Minnesota and the Northwest. One of its first settlers was a doctor who won the dubious distinction of being the first white man to die within its boundaries and probably the first physician to die within the state of Minnesota. One of our pioneer physicians was elected president of M.M.A. in 1911 as one of the earlier "rural" presidents. The "Acton Massacre" which shed the first blood in the Indian uprising in 1862 occurred in our county. In later years the colossal Land O' Lakes started with the Litchfield creamery as its Number One unit under the guiding hand of John Brandt, one of our native sons.

Meeker County was chosen as the first political unit in the United States to be organized for bovine tuberculosis testing to eradicate the spread of tuberculosis to humans from this source. Again, our county was chosen as the first unit to conduct a free Mantoux test for all inhabitants. This, again, was number one in the United States. Apparently some of these things came about because our county can be roughly located as being one-third the distance from the southern boundary of the state in a northerly direction and one-third the distance from the eastern boundary westward. This gives it a central and rather cross-sectional location for an average Minnesota county.

The county is thirty miles from north to south and twenty-four miles from east to west. It includes seventeen and one-half congressional townships. It is roughly 1,200 feet above sea level and consists of sandy loam of remarkable fertility. The eastern, western, northern, and southern portions are wooded and rolling with smaller hills, but the central portion is a flat sandy area, the first indication west of the Mississippi of the great prairies to follow if one journeys westward.

At present diversified farming is basically the economy, but in the early years fuel wood, railroad ties, and wheat were paramount in supporting its people.

Meeker County was created by the seventh territorial legislature of Minnesota,

February 23, 1856. Some changes were later made in its boundary by annexing land from Renville County and relinquishing land to Kandiyohi County, but since 1869 the boundaries have become permanent.

At present the population is some twenty thousand people, with Litchfield the county seat and centrally located. Our name derives from the Honorable B. B. Meeker, a judge of the courts in Minneapolis.

In the words of Hon. A. C. Smith: "Why or wherefore is unknown, unless indeed, the Italian (sic) climate of the 'big prairie,' the richness of her soil, and the beauty of the surroundings were found typified in the geniality of the judge's temperament and the quiet good natured rotundity of his person."

According to the historians, Meeker County was probably not penetrated by La Verendrye, Hennepin, Radisson and others, though doubtless the products of this area were seen and appreciated by the courts of France. On government maps accompanying the official report of J. N. Nicollet and J. C. Fremont in their surveys of the hydrographic basin of the Mississippi in 1842, we find Meeker County to have been a part of the reservation for different sub-Indian bands. This was termed M-de-wa-kan-ton country. Nicollet recognized it as possessing the most beautiful lakes in Minnesota, and hence the name Kandiyohi was given to our western neighbor county, which is the Indian term for beautiful lakes, and originally included in our area. Early French maps alluded to this area as the "Coteau du greene Bois," a plateau heavily wooded and the height of land between the Minnesota and Mississippi drainage basins.

Access would only have been by canoe through the ramifications of the Crow River. This mild-flowing stream divides into two branches, the north and the south, just east of our boundaries; and the north branch originates in Stearns County to our northwest, while the south branch starts in Kandiyohi County to our west. Beaver and other fur-bearing animals were very prevalent in this area in the early days, and the Sioux understandingly were exceedingly reluctant to relinquish these hunting grounds to the "pale faces."

From St. Paul on westward the "Big Woods," as it was called, extended all the way to Meeker County. This was a huge hardwood forest, broken only intermittently by meadows and channels of small streams. However, at Meeker County the terrain changed and prairies took over in the central and western portions of our boundaries. This had much effect on the early colonization, for all one had to do was turn over the soil and plant. Eastern reaches, however, required much grubbing and land clearing before a crop could be raised. This wood was essential to build cabins and still can be found on eminences thorughout the county.

Apparently the first permanent settlers arrived in September, 1855. Interestingly enough, they came in search of pine woods to aid in supplying lumber for the rapidly expanding needs of our young country. John W. Huy and Ben Brown poled a canoe up the Crow (Hasson) River as far as the present site of Forest City, which was later to become the county seat. They erected a cabin, staked claims and a town site, and remained. The first farming operation was performed by Benjamin Dorman when he "broke sod" and planted in 1856 on his farm east of Forest City.

In the autumn of the same year **Dr. Frederick Noah Ripley** arrived overland from Shakopee via Glencoe in company with John McClelland and established a temporary camp at Cedar Lake (Red Cedar Island Lake in Indian lore). They filed claims here and expected to remain, contingent upon the arrival of supplies by wagon in the early spring.

Previous to their arrival in Meeker County, the doctor had resided in Shakopee

at the "Warren House" from September, 1853. He had been educated in New York City and had left his mother and fianceé there when he started his pioneer trip. In 1855 he had so favorably impressed the territorial authorities in St. Paul with his "refined and gentlemanly appearance" that he was notified, pursuant to his filing a claim in Meeker County that year, that he would be appointed a county commissioner in the newly organized county of Meeker. He was a "regular" doctor and anticipated practicing medicine in the usual manner in the growing community of Meeker County and expected to be married as soon as he could establish his house. His fianceé later became a school teacher in Glencoe.

On March 1, 1856, he and McClelland undertook a journey to the home of John Huy and Ben Brown. This, of course, was on foot and covered about eighteen miles each way, and was made because their supplies were low. They had been living in a rough "lean-to" shelter with the knowledge that ample supplies were always available in the cabin of Mr. Huy and Mr. Brown as arranged previously. Let us follow the words of an early historian, Attorney A. C. Smith, in *A Random Historical Sketch of Meeker County,* pp. 114-117:

"It was a delightful morning—the sun shone brightly and the snow was melting fast till 9 a.m. when a gentle breeze from the north-west started up—in a short time clouds began to appear and by 12 a full-grown BLIZZARD was upon them.

"They traveled as near a north-west course as they could calculate, until dark when they stopped in a small popple grove; gathering a pile of dry sticks, with which they started a fire, they camped for the night. . . . Imagination will tell how they spent the night, without food or blankets, and the thermometer down to 20 below and the wind blowing a hurricane, their only occupation was to hunt wood and keep up the fire till morning when they again started out, as was supposed in a direct course for Forest City and traveled until about 9 o'clock a.m. through snow from one to three feet deep before striking Crow River, but whether above or below Forest City they could not tell, and after a search for several hours both up and down stream the Doctor became discouraged and both started to go back whence they came—this was about two p.m.—by this time the storm had abated and the sun came out just before night.

"About dark they accidentally came to the place where they had camped the night before, but to their great disappointment the fire had gone out and their few remaining matches were found to be wet, they had no fire and as they started out without food, in anticipation of getting through to Forest City the same night, hunger and cold told on them terribly. The Dr. was badly chilled—both walked the grove for some time but concluded to strike out for camp as it was quite as easy to walk on the prairie as in the timber.

"Ripley showed signs of fatigue and quite frequently wanted to stop and rest—McClelland insisted it would not do to stop as he would freeze and McClelland was already aware that his own feet were partially frozen.

"Ripley was evidently freezing as at every step he seemed to get weaker and less able to proceed and finally fell down in the snow—McClelland helped him up and led him on for some distance, until Ripley said "Mc. go ahead and if the teams have come into camp—have them come after me.'

"McClelland very reluctantly left Ripley and made as rapid steps for camp as possible, knowing full well that he was taking a last farewell of the good man on earth.

"McClelland left Ripley about a mile from what is now called Lake Ripley.

"The Dr. seems to have wandered back to the grove, where his remains were found in the April following by Mr. William S. Chapman (now of California.)

"McClelland left Ripley about 8 o'clock a.m. of the third day out and seven miles from camp. McClelland had a hard day's work and got into camp about sun down with his feet badly frozen, where he lay nineteen days before the expected team arrived. Dr. Ripley was thirty-two years old.

"When McClelland was discovered in camp, he was in a dreadful state of prostration, was immediately removed to Shakopee and both legs amputated above the knee."

McClelland surmised that Dr. Ripley's remains were devoured by wolves as he himself had experienced difficulty in keeping the wolves off while in the cabin.

A few notes taken from the local *News Ledger* are instructive:

June 26, 1873: "The body of Dr. Ripley who froze to death on the prairie between Round Lake and Lake Ripley is to be disinterred soon and buried in Ripley cemetery."

June 28, 1878: "Burial services Sunday, June 16th. Reburied Dr. Ripley by Masonic Lodge. Burial Services: Frederick Noah Ripley, The first white man who died in Meeker County.

"On Monday last a committee appointed by the Masonic order of this place reported to the spot where Dr. Ripley was lain 22 years ago last April and exhumed the remains for a more fitting internment in a lot which had been set aside by the cemetery association for that purpose. Dr. Ripley's remains were found and buried by William S. Chapman in April, 1856. His grave was beneath an oak tree a short distance southeast of the residence of Ole Johnson and tradition informs us that his frozen corpse was found in a half-sitting posture at the foot of the tree under which he was buried. The remains were found in a better preserved conditon than was expected, the bones being all in a perfect state of preservation. A fitting casket was procured by the lodge and the remains were carried to the Masonic Hall to await the burial ceremony on Sunday last.

"At two o'clock the Masons assembled and formed in due and ancient style and headed by the Litchfield brass band and followed by quite a procession of citizens, escorted all that was left of Dr. Ripley to the cemetery. At the grave the usual Masonic services were held: the white apron and sprig were dropped upon the remains, and Dr. Ripley now sleeps in an honored grave on the banks of the beautiful lake that perpetuates his name.

"The following very appropriate remarks were made by P.W.M. Judge A. C. Smith as the remains were consigned to their last resting place:

" 'My brethren! The occasion which calls us together is of no ordinary character.

" 'Among the many incidents pertaining to the settlement of a new country, there are none which appeal to the better sympathies of humanity than those which apply to the hardships of the ones who first take possession of the new Eldorado.

" 'We today deposit in the central rotunda of the Litchfield cemetery the remains of brother Frederick Noah Ripley.

" 'Of the history of Brother Ripley, it is unnecessary for me to speak; it has passed upon the record and become a portion of the permanent history of Meeker County. The name attached to yonder beautiful lake will be thus preserved through coming time.

" 'Twenty-two years ago, the frail tenement, represented today by the remains before us, gave up a valuable life on this then boundless and unsettled prairie; pillowed upon the snowbank—lost to the world—thousands of miles from relations, and hundreds of miles from friends. God only knows the sufferings of a man in like circumstances; and why it was that the talented and accomplished Ripley should be required to lay down his life, on this spot, in the bloom of early manhood, must forever remain a sealed book to mortal eyes.

" 'Suffice to say, Brother Ripley fell in with the then current of immigration and, while he was among the first to interest himself in the settlement of central Minnesota, he was the first to surrender life on this vast prairie.

" 'He died on the third day of March, 1856; and about the middle of April following, his remains were discovered by William S. Chapman, then of Minneapolis, now of California, who came to Forest City, and with the assistance of James Quick, Dudley Taylor, Matt Standish, and Rudolph Schultz, a plain coffin was provided from the scant material then to be had and a decent burial was given him in yonder grave. That narrow and somewhat homely tenement he has occupied for twenty-two years.

" 'In the meantime our county is covered over with the civilization of the age; Meeker and Kandiyohi counties now shelter more than twenty thousand inhabitants, from all parts of the civilized world. Our fields teem with the richest gifts of Ceres; luxurious dwellings now adorn our hillsides and peep from numerous groves surrounding beautiful lakes, and the stranger is entranced as he silently gazes on the scene spread out before him. Railroads pass us, over five hundred miles and we are in daily communication with all civilized countries of the globe.

" 'A town (Litchfield) has sprung up but a single mile from the cheerless death bed of Ripley, now containing twelve hundred inhabitants with five church edifices pointing to the sky, and with a Masonic Lodge of over seventy-five members, and it well becomes us, although at this late day, to pay this tribute to the memory of our deceased brother.

" 'My brethren! The obligations of Masonry are never circumscribed by the statute of limitations and should the kindred of our brother ever learn of this deep doings, it may be a consolation to them to know that the emblems of innocence and immortality have been

strewn with a liberal hand over the final resting place of our brother by Golden Fleece Lodge Number 89, A.:F.: and A.:M.:

"'My brethren, we have searched for and found the remains of our deceased brother, and here deposit them in the Temple of the Dead in form and with the ancient solemnities of our order, ever bearing in mind that the little line that divides the living from the dead is narrow and brittle and on either side lie the tragedies of human life and all of the mysteries of the future.'" . . . A. C. Smith, P.W.M.

Perhaps it would be well at this time, namely 1873, to glance at the county again. The lands had been largely settled throughout its reaches.

The largest village was the county seat of Litchfield in the center of the county. Eden Valley was just being established astraddle the county line in the north central boundary. Darwin was a growing village seven miles east of Litchfield, and Dassel well established twelve miles east of Litchfield. Cedar Mills was a thriving hamlet eleven miles to the south of Litchfield, and Swede Grove or Grove City, eight miles to the west. There were post offices in Kingston in the northeast corner of the county, Forest City (the original county seat) seven miles northeast of Litchfield, Manannah thirteen miles northwest of Litchfield, Crow River five miles west of Manannah, Rosendale nine miles south of Grove City, Cosmos southwest of Grove City sixteen miles, Greenleaf eight miles south of Litchfield, Cedar Mills four miles south and west of Greenleaf, Bonniwell Mills, in the extreme southeast part of the county, and Collinwood four miles southeast of Dassel. These inland towns, having no railroad, had stage coach service regularly from one to six days per week.

Immigration had been principally from native-born "Yankees" of the eastern seaboard states during the fifties and sixties, but an abrupt change had begun by 1870. Irish settlers had developed a community at Rice Lake (now Darwin) and had communicated with their friends and relatives, who in turn arrived in ever larger numbers. Germans had found the townships of Greenleaf and Ellsworth much to their liking, and the same process had taken place there. Norwegians and Swedes came and settled throughout the county but with perhaps the greatest numbers in the central and western portions. Indeed, Grove City was originally called "Swede Grove" on that account, and a township still carries that well-deserved appellation. Later still a large group of Finnish people established their homes in the northeastern corner of the county, principally in Kingston township.

Consequently, we are a well-mixed cosmopolitan race and justly proud of it. Intermarriage has naturally taken place, and minor groups and individuals including French, Indians, Bulgarians, Mexicans, Jewish, and Armenians, to mention a few specifically, have lived in and enjoyed the benefits of Meeker County citizenship. Perhaps the most interesting thing about the settlement of our county can be stated in this manner: Anyone coming here in pioneer fashion expected to have to work hard and build his own future with his own hands. His future and that of his progeny was assured if he was willing to combat the elements and take advantage of the productivity that nature provided. Of necessity he had to be strong physically, self-reliant, careful and frugal. These characteristics are typical of any Minnesotan today.

These pioneers of many extractions took their place well in the Civil War. The G.A.R. (Grand Army of the Republic) was well organized in Litchfield and in 1883 built and consigned their building to the city of Litchfield. Again, we must state that this was another first for Meeker County, inasmuch as this was the only meeting place owned by the G.A.R. in the entire state of Minnesota. At the outbreak of the Rebellion of 1861 there were twelve hundred inhabitants

in Meeker County, and in summation we find two hundred forty-nine men who were regularly inducted as soldiers from this county. This probably is also a record.

Naturally, one looks for an explanation of such a situation, and it is readily available. The bloody Indian uprising of 1862 started in Meeker County. The Indians under Little Crow had been harassed and brow-beaten, always shunted farther westward, and Meeker County was at that time a frontier of farmers that extended into the Indian country. Let us again follow an early historian, A. C. Smith, in *A Random Historical Sketch of Meeker County*, p. 38 ff.

"The Indian War formed a tragical episode in the history of Meeker County.

"About 11 o'clock a.m., of Sunday, the 17th of August, 1862, the first deliberate massacre of the brutal Sioux outbreak, took place thirteen miles west of Forest City in the town of Acton.

"Six Indians came first to the house of Robinson Jones, and thence to that of Mr. Howard Baker, where they deliberately shot five persons, viz: Robinson Jones, Howard Baker, Mrs. Ann Baker, Viranus Webster and Miss Clara D. Wilson, (the last named, at Jones' house). This was the commencement of that terrible Indian scourge, which resulted in the massacre of about nine hundred whites, on the frontier of Minnesota in the fall of 1862.

"The preliminary tragedy at Acton, was not the result of a drunken riot—but was the commencement of a premeditated design to exterminate the whites from this region of country, although probably this early commencement, by an insignificant band, was not a part of the programme of Little Crow and other leaders. I allude to this, to correct errors which appear to have already been manufactured into departmental history. The Secretary of War reported to Congress, and all the pretended histories yet written, CRAW FISH to the fur traders, and allege a drunken broil as the commencement of the affair, and also make statements credited to the reports of a child afterwards found in Jones' house on the eve of the 17th, about 8 o'clock. Mr. John Blackwell, a reliable citizen, now deceased, found a little grandchild of Mrs. Ann Baker, eighteen months old, on the floor in Jones' house (the only one left or found in the house) and took it away—this child was too young to talk and was totally unconscious of its tragic surroundings.

"It was lying upon the floor where it appeared to have cried itself to sleep.

"Whether the Indians considered the child too insignificant to kill, or did not see it at all, cannot be known, the latter supposition is probably correct.

"One writer says that the child lay on the bed and witnessed the scalping of his sister, but this is a mistake. The bed had not been tumbled and no other act done indicating that the Indians ever went into the house, and the girl had not been scalped or mutilated in any way but lay partly upon her back in a pool of blood just where she fell.

"After Baker and Webster ceased to breathe, their wives started for the house of Mr. John Blackwell, their nearest neighbor, Mrs. Baker carrying in her arms an infant child preserved from the massacre.

"When they reached Blackwell's they found no one at home, and proceeded on to the next neighbor, named Olson, a blacksmith, whom the Indians afterwards killed.

"Late in the afternoon Blackwell, on horseback, came riding leisurely home, and learned from Ole H. Ness, Esq., whom he met on the prairie, the terrible news, which he at first could not believe, but Mr. Ness advised him to go to the house of Olson where the women then were and learn the particulars from them which he did, and learned from them that their husbands were dead before they left the house, and that two other persons, Robinson Jones and Mrs. Baker (mother of Howard Baker) were both shot, were both in great agony and evidently dying; that Mrs. Baker was lying in the house and Jones in the yard near the house; that the latter came there from his own house but a short time before where he had left the said niece and child.

"The fate of those children was then problematical, fearing the worst, the Indians having gone in that direction, Blackwell concluded at once, that to find out what had become of them was an imperative duty, and immediately rode back to where he had left Ole H. Ness and found him with Henry Halverson, A. Nelson Fosen, and several others who had assembled and were discussing the matter.

"The men were all in favor of going at once to the scene of the tragedy and securing, if alive, the girl and child.

"It was after dark when they arrived at Jones house and the child was found alive—the remainder of the story has been told, and needs not to be repeated.

"The child was brought to Forest City and kept some months by Mr. and Mrs. Jewett and subsequently placed in charge of Mr. Charles H. Ellis of Otsego, Wright county, since which time we have lost track of him.

"Jones gave the Indians no liquor, and while there was liquor in Jones' house, up to the time of the inquest on Monday afternoon, there was no appearance of its having been molested. At the time of the inquest all the liquor in the house was poured on the ground.

"To show the evident design of these Indians to commit the tragedy at this point, we give the testimony of the wife of Mr. Howard Baker at the coroner's inquest conducted by A. C. Smith, the Judge of Probate and acting County Attorney. Her testimony was as follows:

" 'About 11 o'clock a.m. four Indians came into our house, staid about fifteen minutes, got up and looked out, had the men take down their guns and shoot them off at a mark, then bantered for a trade with Jones. About 12 o'clock two more Indians came and got some water; our guns were not reloaded; the Indians loaded their guns in the dooryard; I went back into the house, did not suspect anything at the time; supposed they were going away; next I knew I heard the report of a gun and saw Webster fall; he stood and fell near the door; another Indian came to the door and aimed at Howard Baker and shot; did not kill him at that time; he shot the other barrel of his gun at Howard and he fell.

" 'My mother walked to the door and another Indian shot her; she turned to run and fell into the buttery; they shot at her twice as she fell. I tried to get out of the window, but fell down cellar; saw Mrs. Webster pulling her husband into the house, don't know where she was prior to this; Indians immediately left the house; while I was in the cellar I heard firing out of doors.

" 'Jones said they were Sioux Indians and that he was well acquainted with them. Two of the Indians had on white men's coats; one quite tall, one quite small, one thick and chubby and all middle aged Indians, one had two feathers in his cap and one had three. Jones said "they asked me for whisky but I would not give them any".'

"This testimony shows a deliberate intention to massacre Jones' family. The facts are that Robinson Jones kept a sort of frontier public house and kept various articles of groceries, etc., with which he used to traffic with the Indians, with whom he was well acquainted, and obtained their furs and other proceeds of their hunting expeditions, and they had by some means got into his debt 40 or 50 dollars, which sum Jones had made arrangements to have paid out of their annuities.

"Certain Indian traders claimed the monopoly of the fur trade, and had for some years been in the habit of making advances to the Indians with the understanding that the Indians were to return to the traders the proceeds of the chase—the balance if any to be jerked (in a manner only known to Indian traders) out of the next succeeding annuities.

"Jones' little traffic was interfering quite materially with those traders, and was setting a bad precedent, and this may, perhaps, furnish a better clue than whisky, to the destruction of Jones' family, and which in its results, produced far more than the traders bargained for. The Indians were dissatisfied with all the traders, and Jones with the rest.

"Any one who understands the Indian trading system, as sanctioned by the Indian Department at Washington, can fill up the balance of the picture—those who do not, will never know any more about the origin of the Indian massacre than they do now.

"On Monday morning the 18th of August, news of the Acton massacre reached Forest City, and in less than an hour A. C. Smith, J. B. Atkinson, Milton Gorton and a few other accompanied by Mrs. Gorton and Mrs. Jewett, were on their way to the scene of the tragedy—with increasing numbers they arrived at Acton some sixty strong—held an inquest and buried the dead. On their return in the evening, the whole community was in a panic and appeared to be in Forest City.

"There were various men among our people, who 'lived fast,' between the 17th of August and the 4th of September, 1862—some in tragedy and some in comedy—far more peril to individuals than to companies of men, assembled for mutual protection.

"We could wish that we had a sketch of all such, including the hair-breadth escapes of men and families; but the facts are not furnished us, and we cannot do justice to the parties in interest from rumors obtained at the time, or from our recollection of circumstances." (pp. 58-59, *History of Meeker County*).

"On the 24th of August, Capt. Strout was ordered to Forest City via Glencoe and Hutchinson but deeming Forest City the safest place, from his stand point, came up the Mississippi direct to the latter place, arriving on the eve. of the 27th, and went into camp near the law office of Judge Smith." (p. 64, *History of Meeker County*).

"There were twelve persons killed in Meeker County and twelve in Monongalia the names

of which were, in Meeker, Robinson Jones, Ann Baker, Viranus Webster, Clara D. Wilson, Philip Deck, Joseph Page, Linus Howe, Wilmot Maybee, Nels Olsen, Caleb Sanborn and Cross, and in July, 1863, James McGannon. In Monongalia three Olsen's, father and two sons, Anderson and son, Carl Carlson and son, Mr. Backland, Mr. Lawrenson and the Lumberg family, and nine in McLeod County, contiguous to Meeker, viz: Mr. Spondy, wife and two children, one child of John Adams (taking John Adams prisoner) and four of the White family at Lake Addie. Mr. Adams was taken prisoner Sept. 4.

"Total killed in Meeker and vicinity, thirty-three, and probably some who have never been reported.

July 1, 1863, McGannon was shot between Kingston and Fair Haven, probably by Little Crow in person, as this distinguished chieftain was a few days after shot by Mr. Lamson on section 30 Town 118-29 (Collinwood) Meeker County, and was found in possession of McGannon's coat.

"The great native warrior, together with his son—young Crow—were quietly making a dinner of raspberries, when the Irishman's bullet called him to his final account." (pp. 82-83, *History of Meeker County*).

This then gives us a background in the struggle for a pioneer's livelihood. Let us visualize a few of the other obstacles.

In 1873 we have the story of a natural catastrophe which is best described in the words of a paragraph in the *Minneapolis Journal* of January 7, 1953:

"TODAY MARKS ANNIVERSARY OF '73 BLIZZARD. Today is the anniversary of the great blizzard of 1873. It was known for sustained fury. For fifty-two solid hours an unrelenting wind blew, piling up huge drifts and cutting visibility to zero.

"The blizzard was especially severe in the Red River valley and southwestern Minnesota, where three days of storming were reported. It followed a succession of steady snowfalls and erupted after calm weather had given many farmers opportunity to get to town. Many of them were caught by the storm.

"Seventy persons died in the state. In one case a boy who started from school for his home across the road was found frozen to death eight miles away. The summer of 1873 wasn't so good either. It saw the state's first great infestation of locusts."

(To be continued in July issue)

MINNESOTA BLUE CROSS-BLUE SHIELD

Minnesota Blue Shield has experienced greater increases in the number of Medical Service Reports submitted during 1957 and the first two months of 1958 than during any similar period in the Plan's history.

During 1956, Blue Shield received 212,828 of these claim forms, for a monthly average of approximately 17,700 while during 1957 more than 260,000 reports were received for a monthly average of over 21,600 claims. This monthly average figure is more than 22 per cent greater than the monthly average for the year 1956. During January and February of 1958, over 48,000 of these reports were received, an average of 24,000 reports each month. This figure is approximately 11 per cent greater than the monthly average number of reports received during 1957.

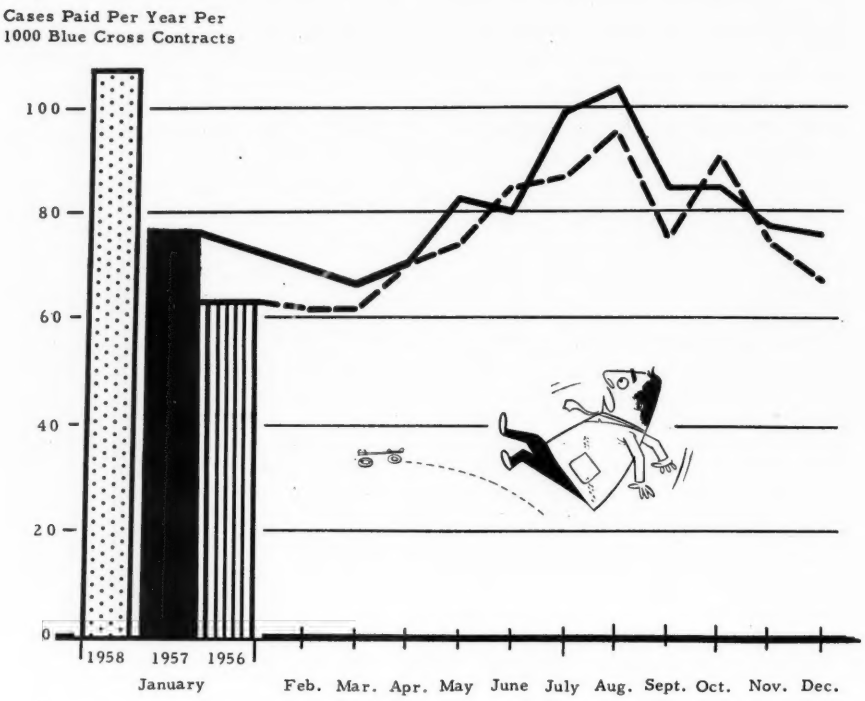
Blue Shield enrollment experienced an increase of approximately six per cent in the period between December 31, 1956, and March 1, 1958. However, increased enrollment alone does not account for the increased number of Medical Service Reports submitted. The increased number of claims submitted is principally due to increased utilization of the contract and increased incidence of services.

Blue Shield benefits are provided for services reported on well over 90 per cent of the reports submitted. Less than ten per cent of all claims received are rejected or forwarded to other Blue Shield Plans. However, all claims received require at least limited processing.

While the Blue Shield work-load increased greatly during 1957, and again during January and February of 1958, the number of employes has not been increased. Improved methods have enabled the Claims Department to process the increased number of claims, well over 1,000 each working day, without additional help.

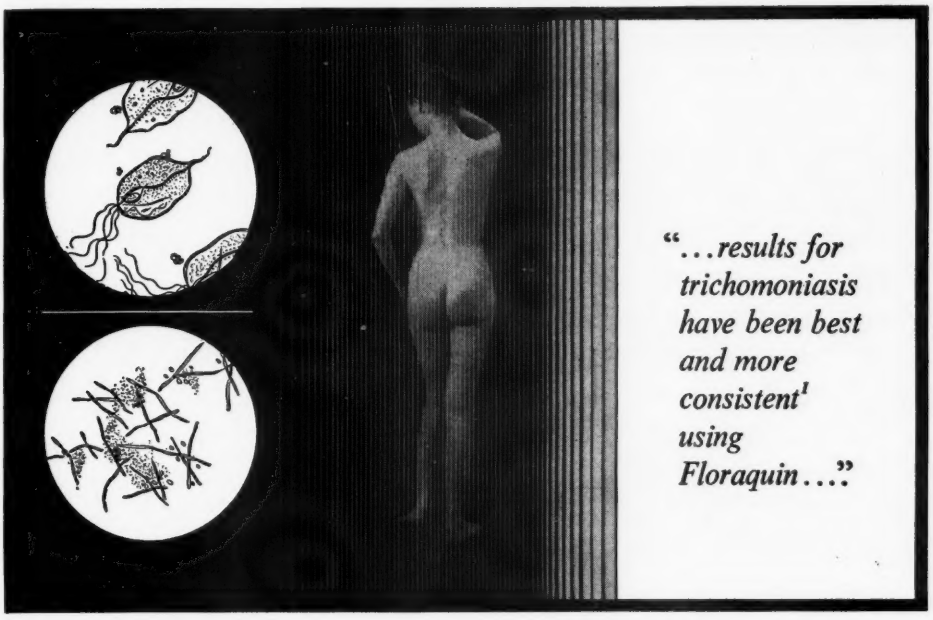
During the year 1957, Minnesota Blue Cross provided hospitalization benefits for nearly one out of every two contracts in effect. This experience marked a new high in frequency of subscriber usage of Blue Cross benefits.

TREND OF ACCIDENTS INCURRED BY BLUE CROSS SUBSCRIBERS



(Continued on Page A-42)

EFFECTIVE, DEPENDABLE THERAPY FOR VAGINITIS



Floraquin® eliminates trichomonal and mycotic infection; restores normal vaginal acidity

Leukorrhea is by far the most frequent symptom of vaginitis; trichomonads and monilia are the most common causes. Many authors have reported[2] trichomonal protozoa in the vagina of 25 per cent of obstetric and gynecologic patients. Increased use of broad spectrum antibiotics has resulted in a sharp rise in the incidence of monilial infections.

Floraquin effectively eradicates both trichomonal and monilial vaginal infections through the action of its Diodoquin® content. Floraquin also furnishes boric acid and sugar to restore the normal vaginal acidity which inhibits pathogens and favors the growth of protective Döderlein bacilli.

Pitt[1] recommends vaginal insufflation of Floraquin powder daily for three to five days, followed by acid douches and the daily insertion of Floraquin vaginal tablets throughout one or two menstrual cycles. G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

---

1. Pitt, M. B.: Leukorrhea. Causes and Management, J. M. A. Alabama *25*:182 (Feb.) 1956.
2. Parker, R. T.; Jones, C. P., and Thomas, W. L.: Pruritus Vulvae, North Carolina M. J. *16*:570 (Dec.) 1955.

SEARLE

Rugged or Restful as you please...

MANITOBA

CANADA'S

Land of Vacation Contrasts

Learn what relaxation really means—in Manitoba! Here you can take in the sun on sandy beaches . . . swim, play golf, sail . . . and FISH! Over 39,000 sq. mi. of lakes, streams and rivers teeming with fighting fish await your pleasure.

Bring the family—there's fun for all! Main highways are excellent . . . modern accommodation is available at reasonable rates.

To help you plan your trip to Manitoba, this 48-page color-packed booklet is free for the asking. Mail in the coupon today! 8012

Bureau of Travel and Publicity,
851 Legislative Building,
Winnipeg, Manitoba, Canada

Name _____

Street _____

City _____ State _____
(PLEASE PRINT)

MINNESOTA BLUE CROSS-BLUE SHIELD

(Continued from Page 290)

January, 1958, experience indicates a continuation of the 1957 high-incidence trend. Over 18,000 subscribers were provided 112,239 days of hospital care during the month. The incidence rate represented is 513 cases paid per year per 1,000 contracts protected—over one out of every two contracts protected—a five per cent increase over the frequency of Blue Cross usage during the previous January. Each hospitalized subscriber stayed an average of 6.2 days, an increase of two-tenths of a day compared with the average length of stay during January, 1957.

Accidental injuries and poisonings led all other reasons for hospitalization of Blue Cross subscribers with 3,784 admissions representing 20.8 per cent of all cases paid during the month of January, 1958. The frequency of incurrence of such cases reached a new high—with 107 cases paid per year per 1,000 contracts protected—a 40 per cent increase in frequency compared with the previous January.

The normal trend of incidence of accidental injuries and poisonings is an increased rate over the summer months of the year as compared with the winter months—rather the reverse of the trend in frequency of respiratory illness occurrence. However, as seen in the chart above, January, 1958, experience exceeds that of the highest peak of the preceding two years' Blue Cross experience.

Pregnancy ranked third in reasons for hospitalization of Blue Cross subscribers with 2,638 admissions representing 14.5 per cent of the cases paid during January, 1958. These cases required 12,453.3 days of hospital care, an average of 4.7 days per case.

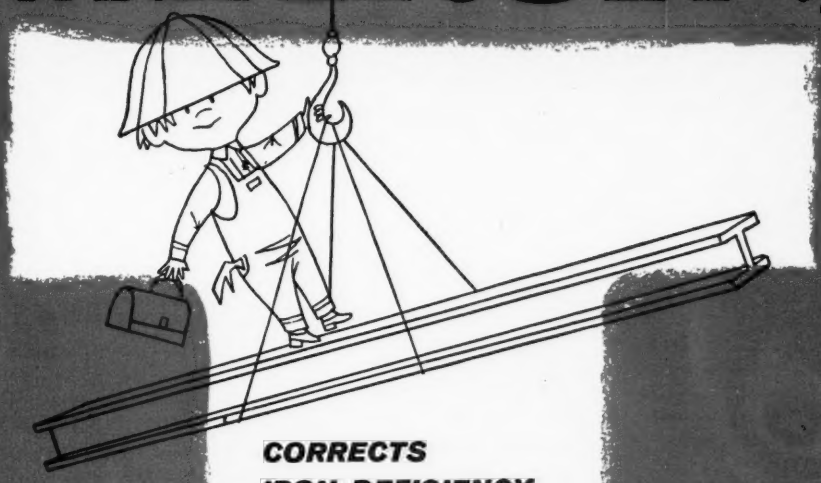
Diseases of the respiratory system continue to be a leading factor in Blue Cross utilization. During January, 1958, the second leading cause of subscriber hospitalization was respiratory illnesses. The 2,974 admissions involved representing 16.3 per cent of all cases paid required 14,224.7 days of care, an average of 4.8 days per case.

Although the high frequency of hospitalization for respiratory illnesses is continuing, the incidence rate of 84 cases paid per year per 1,000 contracts protected is not excessively high for this season of the year. It is interesting to note that the average hospital stay has decreased from 5.3 days and 5.5 days per case during November and December, 1957 respectively to 4.8 days per case during January, 1958.

Social security has been changed many times in the twenty-two years since the original law was enacted. The size and variety of benefits, the tax rates, the tax base, coverage—all have been radically changed. There is no reason to believe that another twenty-two years will not see just as radical changes.

new INCREMIN* with IRON syrup

LYSINE-VITAMINS



CORRECTS IRON DEFICIENCY AS IT STIMULATES APPETITE

DELICIOUS CHERRY FLAVOR DESIGNED TO APPEAL TO BOTH CHILDREN AND ADULTS

PARTICULARLY FOR CHILDREN

Supplies essential Iron as ferric pyrophosphate, highly stable, well-tolerated, readily absorbed; essential vitamins B_1, B_6 and B_{12}, established as appetite stimulants; essential l-Lysine for greater protein economy in the pediatric diet.

INCREMIN Syrup

FORMULA: Each teaspoonful (5 cc.) contains:

l-Lysine HCl	300 mg.
Ferric Pyrophosphate (Soluble)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine Mononitrate (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Alcohol	0.75%

Average dosage is 1 teaspoonful daily.
Available in bottles of 4 fl. oz.

*REG. U. S. PAT. OFF.

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, N.Y.

Meetings and Announcements

STATE

Minnesota Association of Blood Banks, 1958 anuual meeting, in conjunction with the Upper Midwest Hospital Conference, Minneapolis Auditorium, May 14, 1958.

MINNESOTA STATE MEDICAL ASSOCIATION, 105th annual meeting, Minneapolis, May 22, 23 and 24, 1958. Business sessions and exhibits, Minneapolis Auditorium. Headquarters, Leamington Hotel.

Minnesota Surgical Society, spring meeting, Rochester, Minnesota, May 9, 1958. O. H. Beahrs, M.D., Secretary, Rochester, Minnesota.

NATIONAL

American Congress of Physical Medicine and Rehabilitation, 36th annual scientific and clinical session, Bellevue-Stratford Hotel, Philadelphia, August 24-29, 1958.

American Gastroenterological Association, 59th annual meeting, Washington, D. C., May 30-31, 1958. H. M. Pollard, M.D., Secretary-General, University Hospital, Ann Arbor, Michigan.

American Goiter Association, 1958 meeting, June 17-19, San Francisco, California.

First All-Day Forum on Medical Economics, March 27, 1958, Washington, D. C. Co-sponsored by the Medical Council of the Washington Metropolitan Area and the Wm. S. Merrell Company of Cincinnati, Ohio.

Gerontological Society, Inc., Bellevue Stratford Hotel, eleventh annual scientific meeting, Philadelphia, Pennsylvania, November 6, 7, and 8, 1958.

Symposium on "Basal Gangila Surgery for Involuntary Movement Disorders." New York University-Bellevue Medical Center, Thursday, May 15 to Saturday, May 17. Complimentary tickets. Miss Dorothy P. Frome, Office of Public Relations, 550 First Avenue, New York 16, New York.

Trudeau School of Tuberculosis and Other Pulmonary Diseases, forty-third session, Saranac Lake, N. Y., June 2 to 20, 1958. Detailed information may be obtained from the Secretary, Trudeau School of Tuberculosis and Other Pulmonary Diseases, Box 500 Saranac Lake, N. Y.

INTERNATIONAL

Fifth International Congress on Diseases of the Chest, sponsored by American College of Chest Physicians, Tokyo, Japan, September 7-11, 1958.

Third International Congress of Allergy, sponsored by International Association of Allergology and French Allergy, Association, Paris, France, October 19-26, 1958.

World Congress of Gastroenterology, Washington, D. C., May 24-31, 1958. Joint meeting with the American Gastroenterological Association, Dr. H. M. Pollard, Secretary-General, University Hospital, Ann Arbor, Michigan.

LOVELACE FOUNDATION PROGRAM

The Lovelace Foundation, Albuquerque, New Mexico, has instituted a program for Visiting Physicians and Surgeons *pro tem.* The program is intended to further the opportunities for graduate medical education in bringing to practicing physicians, the latest advances of fundamental and clinical medicine and surgery.

The first Visiting Physician *pro tem* was Dr. Arthur M. Olsen, Professor of Medicine, Graduate School, University of Minnesota, and one of the Chiefs of Medicine of the Mayo Clinic.

MEDICAL EDUCATION WEEK

The American Medical Association has announced that it will again join the nation's 83 medical colleges in helping develop and promote the Third Annual Medical Education Week, April 20-26, 1958.

The National Committee on Medical Education Week will send promotional kits to state and county medical societies for use during this week. These kits will contain scripts, speeches, sample proclamations, editorials, and other programs for civic attention.

CONTINUATION COURSES

Medical continuation courses to be presented at the Center for Continuation Study, University of Minnesota are as follows:

April 7-9—Radiology for General Physicians
April 10-12—Arthritis and Physical Medicine for General Physicians
April 12—Trauma for General Physicians
April 14-16—Gastroenterology for General Physicians
May 5-9—Electrocardiography for General Physicians & Specialists
May 12-16—Proctology for General Physicians

For further information concerning the above courses, write to the Director, Department of Continuation Medical Education, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minnesota.

ADVANCED ORAL PATHOLOGY COURSE

The Dental and Medical Faculty of the University of Minnesota will present a course in Advanced Oral Pathology during the week of April 28 through May 2, 1958. Both lectures and pathologic slide study will be included. Microscopes will be provided. The material presented will include: neoplastic and non-

(Continued on Page A-46)

IN ALL DIARRHEAS . . . REGARDLESS OF ETIOLOGY

comprehensive control with **CREMOMYCIN**®

SULFASUXIDINE* PECTIN-KAOLIN-NEOMYCIN SUSPENSION

SOOTHING ACTION . . . Kaolin and pectin coat and soothe the inflamed mucosa, adsorb toxins and help reduce intestinal hypermotility.

BROAD THERAPY . . . The combined antibacterial effectiveness of neomycin and Sulfasuxidine is concentrated in the bowel since the absorption of both agents is negligible.

LOCAL IRRITATION IS REDUCED and control is instituted against spread of infective organisms and loss of body fluid.

PALATABLE creamy pink, fruit-flavored CREMOMYCIN is pleasant tasting, readily accepted by patients of all ages.

*Sulfasuxidine is a trade-mark of Merck & Co., Inc.

MSD

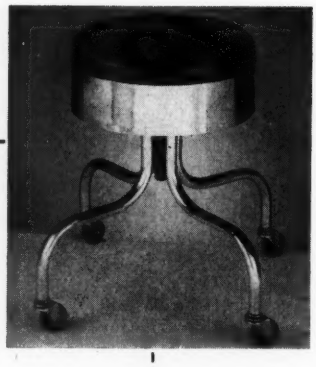
MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

for your

comfort . . .

P & H EXAMINING STOOL

P&H



- Sturdy construction
- Modern design
- Adjustable height
- Naugahyde covering

This stool is built to last. All welded construction. Made of 7/8" gauge tubing. Mounted on 3" ball-bearing swivel casters. Stool is adjustable from 17" to 28". Seat is upholstered in Naugahyde covering of black, brown or gray color. Padded foam rubber seat which can be easily removed.

When ordering specify number MM-458a.

Physicians & Hospitals Supply Co.

1400 Harmon Place ● Minneapolis 3, Minn.

ADVANCED ORAL PATHOLOGY COURSE

(Continued from Page A-44)

neoplastic diseases of the salivary glands, neoplasms of dental origin, bone pathology, soft tissue neoplasms, dermatologic pathology, diseases of the lymphoid system, and oral roentogenographic evidence of systemic disease.

The faculty will include Dr. Robert Lukes, Armed Forces Institute of Pathology, Dr. D. C. Dahlin and Dr. Edward Stafne of Mayo Clinic, Dr. Robert Goltz of the Medical School, University of Minnesota, Dr. Anand Chaudhry and Dr. Robert J. Gorlin of the School of Dentistry, University of Minnesota.

The tuition will be $50 for the week. If room and board at the Center for Continuation Studies are desired, the cost for the week will be about $50.

WARNING TO MINNESOTA PHYSICIANS

An increasing number of Minnesota physicians are falling prey to unlicensed securities brokers both from Canada and New York and other eastern cities by purchasing securities of unknown value.

Arthur Hansen, Commissioner of Securities, has warned that purchase of unregistered securities offered by these out-of-state and out-of-country confidence men who make contact by "hurry up" literature and long distance telephone calls and telegraph messages invariably results in substantial losses to the investor.

From a recent investigation by the Securities Commission of one of these swindling securities dealers, it was noted that eleven of the twenty-six Minnesota victims were physicians who thus far have suffered losses of more than $18,000. As these losses can be avoided, the Commissioner hopes this warning will be kept in mind when physicians are approached by unknown brokers.

Mr. Hansen's office is always available to answer questions concerning securities and a call or a card, when in doubt, to the Securities Division, 202 State Office Building, St. Paul, will save the prospective purchaser money and disappointment.

GOLF TOURNAMENT

The American Medical Golfing Association is holding its annual golf tournament in conjunction with the AMA convention June 23, 1958, at the beautiful Olympic Lakeside Golf and Country Club, San Francisco, California. This will be a whole day of rest and relaxation with golf, luncheon, banquet, and a prize for everyone. No stone has been left unturned to assure participants the very best. Tee off time: 8 a.m. to 2 p.m. All golfing doctors are cordially invited to attend. Handicaps scratch to 30 in flights.

For information, write James J. Leary, M.D., Secretary, 450 Sutter Street, San Francisco, California.

REGISTERED NURSE LICENSURE CHANGES

The Minnesota Board of Nursing announces a change in policy relative to applications for Registered Nurse licensure by interstate endorsement. A nurse licensed elsewhere may not be employed as a registered nurse in Minnesota until she obtains a Minnesota license as such—except while her application for this license is pending. A "courtesy" status is provided while the application is pending for a period *not to exceed six months from the date the application is filed in the Minnesota Board of Nursing office, 700 Minnesota Building, St. Paul 1.* Persons expecting to be employed as registered nurses in Minnesota should request application forms *shortly before* beginning employment in this state.

LABORATORY ASSISTANTS COURSE

The General Extension Division of the University of Minnesota announces that the next course for laboratory assistants will begin July 1, 1958. The twelve-month program trains qualified high school graduates in limited laboratory techniques in hematology, urinalysis, BMR-EKG tests, chemistry, and blood banking. At the end of this time, the students are best qualified to work in a physician's office or to assist a registered medical technologist M.T. (ASCP) in a hospital or clinical laboratory. Further information and application blanks about the program can be obtained from Margaret Ohlen, Instructor and Co-ordinator, Medical Laboratory Assistant Program, C205 Mayo Building, University of Minnesota, Minneapolis 14, Minnesota.

CAMP PHYSICIANS WANTED

The Saint Paul Area Boy Scout Camp is again requesting the services of interested physicians. One-week periods of camp run from June 14, 1958, to the latter part of August. A new cabin with all modern plumbing facilities is supplied to the doctor and his family. Two nurses are on duty at all times at the camp.

For further information, write or call Dr. Donald W. Koza, 1210 Lowry Medical Arts Building, Saint Paul 2, Minnesota. Telephone: CApitol 4-5371.

SYMPOSIUM ON CARDIOVASCULAR DISEASE

Preceding the dedication of the new Lake Region Hospital in Fergus Falls, Minnesota, the medical staff is sponsoring a symposium on "The Frontiers of Cardiovascular Disease." This is to be held on Saturday, June 28, 1958. The faculty will consist of physicians specializing in cardiovascular disease from Rochester, Minnesota, the Twin Cities, and Winnipeg, Canada. All doctors interested are cordially invited to attend. The program will appear in the next issue.

Narone®

●NON-NARCOTIC ●NON-HYPNOTIC

Severe pain is usually controlled immediately and relief sustained as long as eight or more hours following parenteral administration of Narone (Ulmer).

Not a narcotic. Narone does not interfere with routine activities . . . causes no central depression or nausea. It is sedative-free, non-addicting and continued use does not increase tolerance.

Narone is indicated in terminal carcinoma, renal and biliary colic, refractory rheumatic disease, post-operative pain and similar disorders. It may be used for symptomatic relief of painful inflammatory states where steroid therapy is contraindicated. Often oral Narone therapy fully maintains relief. Long term treatment is not costly.

Narone is available for intravenous, intramuscular or oral use.

Write for descriptive literature

THE ULMER PHARMACAL CO.
1400 HARMON PLACE • MINNEAPOLIS 3, MINNESOTA

ULMER

MM-458b

Woman's Auxiliary

ANNUAL MEETING PROGRAM HIGHLIGHTS

The thirty-sixth annual meeting of the Woman's Auxiliary to the Minnesota State Medical Association will be held May 22-24 in Minneapolis. Convention headquarters for the centennial year observance will be the Curtis Hotel. Auxiliary convention chairmen are Mrs. Conrad Holmberg and Mrs. Mancel Mitchell.

Several highlights of this year's annual meeting will include the executive board meeting and luncheon for county presidents and presidents-elect to be held Thursday, May 22. Following the luncheon, guests will tour the Hennepin County Historical Museum, and will climax that afternoon's activities with a tea at the Minneapolis Art Institute. Thursday evening members of the auxiliary and their husbands have been extended invitations to be the guests of the Hennepin County Medical Society at special entertainment planned for the occasion. The annual meeting and luncheon for all doctors' wives is scheduled for Friday noon, May 23. The annual banquet of the Minnesota State Medical Association will be held Friday, May 23, at 7:00 p.m. in the Leamington Hotel in downtown Minneapolis. Committee chairmen for the event stress the importance of making early reservations for the various events of the annual meeting.

NATIONAL AND INTERNATIONAL MEETINGS

The national meeting of the Woman's Auxiliary to the American Medical Association will be held this year in San Francisco, June 25-27. Immediately following the A.M.A. annual meeting in San Francisco, the Hawaii Summer Medical Conference will be held in Honolulu, July 1-3, 1958.

ST. LOUIS COUNTY AUXILIARY

Recent activities of the St. Louis County Medical Auxiliary include:

Presentation of ten dollars to the winner of the Essay Contest sponsored by the Tuberculosis Society.

Awarding of two nurses scholarships of two hundred dollars each.

Presentation of the invitational annual dinner dance for doctors and their wives from Superior, Wisconsin.

Inauguration of a new volunteer service at one of the hospitals—stork photography. In addition, Auxiliary members are serving as volunteers in related public service areas.

AUXILIARIES SPONSOR MEDICAL VOCATIONS TEAS

Mower County Auxiliary

Members of the Mower County Medical Auxiliary were hostesses at a tea January 24, 1958, for sophomore girls of all Mower County high schools interested in nursing or affiliated fields of the medical profession. Mrs. Wallace Anderson, Auxiliary president, was chairman and introduced the speakers for the nursing field; Mrs. Virginia Spongler, Macalester College, and three Minneapolis student nurses, Lois Barta, Abbott Hospital; Marlene Thimigau, St. Barnabas Hospital; Mrs. Alice Peterson, Northwestern Hospital.

Mower County Auixilary members representing medical technology are Mrs. E. C. Sargent, Mrs. James Thomson, and Mrs. R. R. Wright.

Stearns-Benton County Auxiliary

High school girls from the St. Cloud area were guests recently at a nurses' tea sponsored by the Stearns-Benton Medical Auxiliary in the St. Cloud Hospital School of Nursing home. Those attending included: Mrs. C. F. Brigham, Jr., Arleen Dufault, Patricia Murphy, Mary Kay Ployhart, Carol Schwartz, Mary Kay Popp, Judy Maslonkowski, Jean Smoley and Sister Annora, OSB, assistant administrator.

Must all cardiac patients cut down drastically on exercise? Studies show that over 30 per cent of them require no restriction of activity whatever. Approximately another 40 per cent must avoid only severe exertion. In fact, less than 1 per cent require "complete rest."—*Patterns of Disease.*

* * *

Beer may act favorably in heart failure and arterial hypertension and is a welcome addition to a diet poor in salt, says Dr. B. Josephson of St. Erik's Hospital, Stockholm. Patients there are permitted from 300 to 600 milliliters (approximately one to two pints) of beer daily. He says the method has had similar results in Milwaukee, U.S.A. "No comment!" remarks Dr. Morris Fishbein.—*Medical Science,* December 10, 1957.

DANIELSON MEDICAL ARTS PHARMACY, INC.

10-14 Arcade, Medical Arts Building
825 Nicollet Avenue—Two Entrances—78 South Ninth Street
MINNEAPOLIS

PHONES:
FEderal 3-3317
FEderal 3-3318

HOURS:
WEEK DAYS—8 to 7
SUN. & HOL.—10 to 1

THE MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

LICENSE OF RED WING PHYSICIAN SUSPENDED

The Minnesota State Board of Medical Examiners, on February 15, 1958, suspended for a period of three years the license to practice medicine held by Dr. Howard F. Claydon, fifty-two years of age, of Red Wing, Minnesota. Dr. Claydon had previously been charged in a citation issued by the Board with immoral, dishonorable and unprofessional conduct, as defined by law, in that he had procured, aided and abetted a criminal abortion upon a Minneapolis woman. Dr. Claydon had appeared at a prior meeting of the Board and admitted the truth of the charge in the citation, but because Dr. Claydon was undergoing treatment by a physician for a very serious ailment, the Minnesota State Board of Medical Examiners took the matter under advisement at that time and deferred making a decision in regard to the disciplinary action that should be taken.

An investigation by an agent of the Minnesota Bureau of Criminal Apprehension and a representative of the Minnesota State Board of Medical Examiners disclosed that a thirty-five-year-old Minneapolis divorcee, after learning from an examination by a Minneapolis physician that she was pregnant, was driven to Red Wing by a woman companion who pointed out Dr. Claydon's office to her. The patient, in a signed statement, indicated that she paid $250.00 in cash to Dr. Claydon for performing an abortion upon her, and Dr. Claydon admitted that this was true when he appeared before the Board in response to the citation. After returning to Minneapolis, the patient became ill and was hospitalized in a Minneapolis hospital where she passed the fetus.

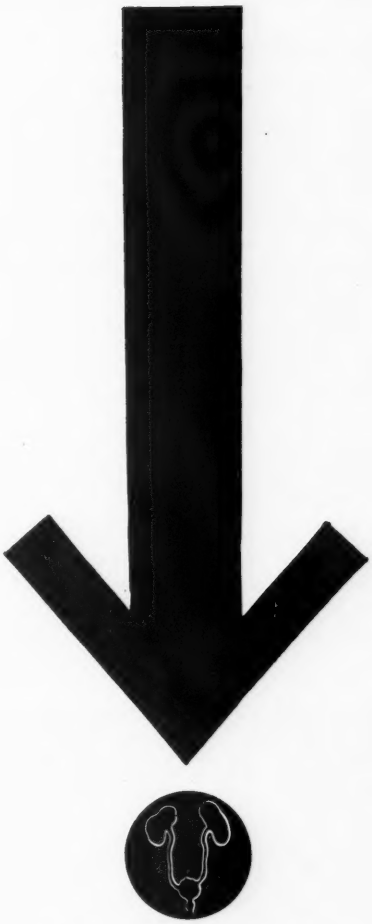
Dr. Claydon, who was born in Red Wing, Minnesota, on October 10, 1905, graduated from the University of Louisville, Louisville, Kentucky, with an M.D. degree in 1929. Dr. Claydon was licensed to practice medicine in Minnesota on December 2, 1930 by reciprocity with Kentucky. Dr. Claydon then entered the practice of medicine at Zumbrota, Minnesota, and remained there until 1947 when he moved to Red Wing.

NEW ULM WOMAN SENTENCED

On March 1, 1958, Marlys Posusta, twenty-seven, New Ulm, Minnesota, was sentenced in that city by the Hon. George D. Erickson, Judge of the District Court, to serve a term of from one to four years in the State Reformatory for Women at Shakopee. The defendant had previously on January 24, 1958, entered a plea of guilty before Judge Erickson to the crime of wilfully producing her own miscarriage and at that time the Court continued the case and ordered that a pre-sentence investigation be made. Judge Erickson granted a stay of execution of the sentence until March 7, 1958, in order to give the defendant time to arrange her personal affairs, but he stated that under the circumstances he did not feel that he would be justified in placing the defendant on probation.

The original investigation in this case, which was conducted by an agent of the Minnesota Bureau of Criminal Apprehension and a representative of the Minnesota State Board of Medical Examiners, disclosed that the defendant had aborted as a result of taking medication and using an instrument upon herself. Miss Posusta became ill after passing the fetus in a friend's apartment in Minneapolis and it became necessary for her to be hospitalized in a Robbinsdale hospital.

When questioned by the Court, the defendant said that she was born on July 26, 1929, at Silver Lake, Minnesota, and that she never married. Miss Posusta, who has no training in any of the healing arts, further stated that she did not attend school beyond the ninth grade but that she had worked in a canning factory at Winsted and had been employed as a waitress in Glencoe.



IN THE MANAGEMENT OF
URINARY TRACT INFECTIONS
YOU CAN BE SURE WITH ®

SUROMATE
patch

NEW TRIPLE SULFA WITH THE DOUBLE PLUS

EACH TABLET CONTAINS:
Sulfadiazine ..... 100 mg.
Sulfamerazine ..... 100 mg.
and
Sulfacetamide ..... 100 mg.
+ Ext. Hyoscyamus ..... 5.75 mg. (alkaloids 0.155%)
+ Potassium citrate ..... 200 mg.

SUPPLIED: Bottles of 100 tablets.

Superior, broad-spectrum antisepsis. Highly soluble, rapidly absorbed, maintains high g.u. concentrations. Effective in low dosage with minimal risk of crystalluria, sensitization, resistance or superinfection.

Prompt antispasmodic and anti-irritant relief of pain and urgency.

Diuresis and alkalization to enhance sulfonamide solubility and safety.

patch THE E. L. PATCH COMPANY
Stoneham, Massachusetts

70 YEARS OF SERVICE TO THE MEDICAL PROFESSION

In Memoriam

RICHARD E. POGUE

Dr. Richard E. Pogue, former Watertown physician, died February 22, 1958, in Carson City, Nevada. He was fifty-three years old. Doctor Pogue was a practicing physician in Watertown for approximately twenty-three years. He retired in 1957.

A native of Duluth, he received his preliminary education at Maplewood Academy. He attended Union College, Lincoln, Nebraska, and Pacific-Union College, Angwin, California.

His medical education was obtained at the College of Medical Evangelists, Loma Linda, California. His special work included internship at Orange County Hospital, Santa Ana, California.

Positions and professional affiliations held by Dr. Pogue include: Superintendent, Cottage Hospital, Watertown, Minnesota; Staff Member, Fairview Hospital and Swedish Hospital, Minneapolis.

He was a member of the Scott-Carver County Medical Society, the Minnesota State Medical Association, and the American Medical Association.

He is survived by his wife, Viola; a son, Richard, Jr., and a daughter, Patricia, all of Watertown.

DONALD R. READER

Dr. Donald R. Reader, St. Paul physician, was killed in an automobile accident February 20, 1958 when his car missed a curve on highway 52, near Dalton, Minnesota. He was forty-six years old.

A native of St. Paul, he received his preliminary education at Cretin High School.

Dr. Reader was a 1958 graduate of the University of Minnesota Medical School. His special work included twelve months' internship at St. Mary's Hospital in Minneapolis.

Dr. Reader was a member of the Incus, honorary medical fraternity; Minnesota Neurological Society, American Psychiatric Association and a diplomate of the American Board of Psychiatry. He was associated with Glenwood Hills Hospital and the mental hygiene section of Veterans' Hospital.

In addition, he was an active member of the Hennepin County Medical Society, the Minnesota State Medical Association and the American Medical Association.

Survivors include his wife Mary; two children, Joanna, seventeen, Thomas, thirteen, and two brothers, Lawrence, Malvern, Pa., and Mark, Minneapolis.

TAKE A LOOK AT
NEW DIMETANE
THE UNEXCELLED
ANTIHISTAMINE

MAGNUS WESTBY

Dr. Magnus Westby, a practicing physician in Madison, Minnesota, died March 13, 1958, while vacationing in Santa Ana, California, at the age of fifty-eight.

In 1955, Dr. Westby was appointed to the State Board of Medical Examiners by Governor Orville Freeman. He held the post as chairman of that board at the time of his death.

A native of Aberdeen, South Dakota, he graduated from St. Olaf College, Northfield, Minnesota, and from University of Minnesota Medical School in 1924. In 1925, he began practicing medicine in Madison.

Dr. Westby served two terms as mayor of Madison. He was a member of the American Legion, Madison Masonic Lodge, Phi Beta Pi medical fraternity, Minneapolis Athletic Club and Faith Lutheran church, Madison. He also was past president of Camp Release Medical Society, the Minnesota State Medical Association and the American Medical Association.

Survivors include two sons, John and Robert, Minneapolis, and five brothers, Sigurd, Willmar; Edmund, Sioux Falls, S. D.; Fritjof, Aberdeen, S. D.; Carl, Culbertson, Mont., and Dr. Peter Westby, Madison.

Forty years ago, according to Health Information Foundation, one in every ten babies born alive in this country was unable to survive the first year of life. Today, the ratio has dropped to one in forty.

Correspondence

To the Editor:

Attention is called to the president's letter in this issue which deals with the Physician's Assistance Committee. I have been deep in organization work during my entire medical career and I believe that this committee is of the utmost importance. I prize most my service as a delegate and I believe the delegate to the House of Delegates of the State Medical Association is the most important man in medicine today. Next I prize most my appointment to the Physician's Assistance Committee. Some committees work hard, some do nothing; some committees accomplish much, some nothing. The Physician's Assistance Committee is working hard and is doing more good for the average practitioner in Minnesota than ever will be appreciated.

Yours truly,
JAMES A. BLAKE, M.D.

Most persons having cancer may, by modern methods, gain months and years of comfortable life when complete cure cannot be obtained.

* * *

About 400,000 new cases of cancer are diagnosed each year.

* * *

Low intensity radium implantation is by far the treatment of choice in oral cavity cancers, with the exceptions of lips and tonsils, where external irradiation can play a considerable role.

Dimetane®
(PARASYMPATHOLYTAMINE MALEATE)
TABLETS (4 MG.), ELIXIR (2 MG. PER 5 CC.) AND EXTENTABS® (12 MG.) UNEXCELLED POTENCY, UNSURPASSED THERAPEUTIC INDEX AND RELATIVE SAFETY. MINIMUM DROWSINESS AND OTHER SIDE EFFECTS.
A. H. ROBINS CO., INC., RICHMOND, VIRGINIA. ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878
Robins

General Interest

A Duluth physician has been honored by the Minnesota Heart Association. **Dr. F. J. Hirschboeck,** one of the founders and former president of the organization, is the recipient of the distinguished service award for outstanding contributions in the field of cardiac health. The award, first ever made by the association in its ten-year history, was presented at the Duluth Covenant Club at a kick-off dinner for the annual Duluth Heart Fund campaign.

* * *

Dr. Alfred Doscherholmen, of the Minneapolis VA hospital, is one of eight recent clinical investigators appointments announced by the Veterans Administration.

* * *

Dr. C. J. Corrigan has joined the consulting staff of the Zumbrota Community Hospital as x-ray specialist. He is also a member of the staff of Olmsted County Hospital in Rochester.

* * *

Dr. F. Henry Ellis, Mayo Clinic surgeon, recently participated in a panel discussion on esophagitis at the sectional meeting of the American College of Surgeons held in New York City.

* * *

Dr. Harold O. Peterson was elected a member of the Board of the American College of Radiology at the annual meeting in Chicago. Dr. Peterson, a graduate of the University of Minnesota and the University's Medical School, will serve four years as a member of the Board of Chancellors.

* * *

Dr. Louis A. Buie, emeritus head of the Section of Proctology of the Mayo Clinic and emeritus professor of proctology in the Mayo Foundation, has been named secretary-treasurer of the Advisory Board for Medical Specialties. Dr. Buie had been acting secretary and treasurer of the board since the death of **Dr. B. R. Kirklin** on March 2, 1957. He has been a member of the board since 1949.

* * *

"The Heart—Its Functions and Malfunctions," was the title of a recent address presented by **Dr. Richard A. DeWall** at a recent St. Paul Junior Chamber of Commerce luncheon.

* * *

At the annual meeting of the medical staff of St. Barnabas Hospital, **Dr. Edgar A. Webb** was elected chief-of-staff, succeeding **Dr. William T. Walsh.** The new Vice chief-of-staff is **Dr. C. R. Peluso** and the secretary is **Dr. D. G. Bohn.**

* * *

Several Rochester men were participants in the 11th biennial International Congress of the International College of Surgeons, March 9-13, in Los Angeles in conjunction with the 23rd annual Congress of the United States and Canadian Sections. **Dr. Henry W. Meyerding,** an emeritus member of the Mayo Clinic staff, is president-elect of the International College. He delivered a paper on "Errors in Treatment of Fractures of Upper Extremities and Their Consequences." **Dr. Winchell Craig,** emeritus Mayo Clinic staff member, and **Dr. Gershom Thompson,** of the Clinic staff, were on the special panel on "Management of Surgical Emergencies." Moderator was **Dr. Ross T. McIntire,** former Surgeon-General of the Navy, now executive director of the International College of Surgeons. Dr. Craig discussed "Injuries of the Head and Spine" and Dr. Thompson talked on "Injuries of the Bladder and Genitalia." Also on the program from the Clinic were **Dr. John Henderson,** moderator of a panel on Symposium on Procedures in Surgical Ophthalmology, and **Dr. A. M. Olsen,** who took part in a symposium on "The Inter-Relation of Pulmonary and Esophageal Diseases."

* * *

Two staff members of the Mayo Clinic were among speakers at the annual clinical conference of the Chicago Medical Society in Chicago. They were **Dr. Hamilton Montgomery,** senior consultant in the section of dermatology, and **Dr. Arthur B. Hunt** of the section of obstetrics and gynecology.

* * *

The new Wright County Medical Advisor is **Dr. G. Harland Purves,** of Buffalo. He succeeds **Dr. Robert M. Sandeen** of that community.

* * *

"Of Thee I Sing; Of Me I Give," was the topic of a recent University of Minnesota Greek Week banquet address given by **Dr. Edward H. Rynearson,** chairman of the section of metabolic diseases at the Mayo Clinic.

* * *

Dr. J. P. Grahek, Ely mayor, has been appointed to the position of the first chief of staff of the medical staff of the Ely-Bloomenson Community Hospital. The announcement was made at the first annual meeting of the shareholders of that corporation. Recently appointed to the staff were **Dr. Edward Ciriacy** and **Dr. Robert Kundel.**

* * *

Three Mayo Clinic staff members recently participated in an international symposium on "Pulmonary Circulation," sponsored by the Chicago Heart Association in the Palmer House at Chicago, March 20-22. They were **Drs. Howard B. Burchell, Jesse Edward** and **John Shepherd.**

* * *

Dr. Douglas L. Johnson has returned to Little Falls following a three-year residency in ophthalmology at the University of Minnesota hospitals. He announced the opening of offices at the Medical Center in Little Falls and at the O'Brien Center in Brainerd. Dr. Johnson's practice will be limited to diseases of the eye and eye surgery. He was formerly in general practice in Little Falls from 1937 to 1955.

(Continued on Page A-56)

ACHROCIDIN*

TETRACYCLINE-ANTIHISTAMINE-ANALGESIC COMPOUND LEDERLE

A versatile, well-balanced formula capable of modifying the course of common upper respiratory infections . . . particularly valuable during respiratory epidemics; when bacterial complications are likely; when patient's history is positive for recurrent otitis, pulmonary, nephritic, or rheumatic involvement.

Adult dosage for ACHROCIDIN Tablets and new caffeine-free ACHROCIDIN Syrup is two tablets or teaspoonfuls of syrup three or four times daily. Dosage for children according to weight and age.

Available on prescription only.

TABLETS *(sugar coated) Each Tablet contains:*

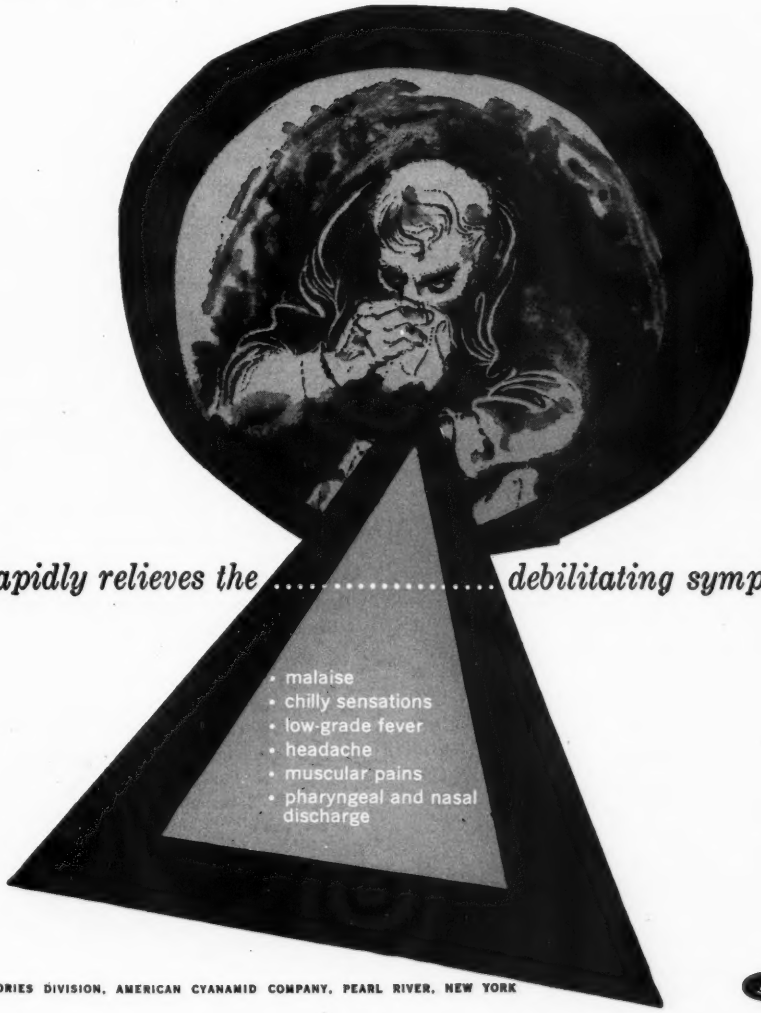
ACHROMYCIN® Tetracycline	125 mg.
Phenacetin	120 mg.
Caffeine	30 mg.
Salicylamide	150 mg.
Chlorothen Citrate	25 mg.

Bottles of 24 and 100.

SYRUP *(lemon-lime flavored) Each teaspoonful (5 cc.) contains:*

ACHROMYCIN® Tetracycline equivalent to tetracycline HCl	125 mg.
Phenacetin	120 mg.
Salicylamide	150 mg.
Ascorbic Acid (C)	25 mg.
Pyrilamine Maleate	15 mg.
Methylparaben	4 mg.
Propylparaben	1 mg.

Bottle of 4 oz.



LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK
*Trademark

Lederle

(Continued from Page A-54)

Members of a recently appointed Poison Center Advisory Committee included the following representatives of state medical and lay groups. Committee members are: **Dr. Frank A. Ubel,** Ramsey County Medical Society; Boris L. Levich, St. Paul Department of Public Safety; **Dr. W. E. Parks,** Minneapolis Division of Public Health; **Dr. Donald E. Roach,** Minnesota Academy of General Practitioners; Glenn I. Prickett, Minnesota Safety Council; Henry Moen, Minnesota State Pharmaceutical Association; **Dr. James Fox,** Minnesota Academy of Occupational Medicine and Surgery; George S. Michaelson, Minnesota Hospital Association, Inc.; **Dr. Tague Chisholm,** Minnesota Academy of Medicine; Mrs. Richard Angevina, Minnesota Congress of Parents and Teachers, Inc.; **Dr. Raymond N. Bieter,** head of the department of pharmacology, University of Minnesota School of Medicine, **Dr. Harold N. Wright,** professor of pharmacology on the University staff, and Harold Brunn, Minnesota State Medical Association.

* * *

Dr. Edward A. Meyerding, well known in the state and nation for outstanding contributions to the cause of public health, retired in April as Managing Director of the Minnesota Tuberculosis and Health Association.

During the first thirteen years of his more than a third of a century as executive of the state Christmas Seal organization, Dr. Meyerding also served as secretary of the Minnesota State Medical Association. Dr. Meyerding resigned from the Medical Association position to devote his entire time to the tuberculosis program.

With the aid of his staff, Dr. Meyerding has built up an organization with approximately 10,000 volunteer workers and many thousands of interested contributors.

"NO, HE'S NOT A DOCTOR. JUST ANOTHER VICTIM OF THE DO-IT-YOURSELF CRAZE."

People in all counties of the state are informed about tuberculosis and health problems through newspaper stories, radio and TV information, literature, conferences, and special courses and through *Everybody's Health,* Christmas Seal magazine.

Under his leadership, the state Christmas Seal organization since 1930 has helped to finance hundreds of tuberculin testing surveys in schools. Mantoux testing, emphasized as the major case-finding program, has in recent years been extended to adults as well as children in community-wide and county-wide surveys.

The Christmas Seal organization has worked closely with the State Medical Association and the Minnesota Department of Health in the accreditation of counties for progress in reducing tuberculosis death and infection rates; in tuberculin testing and in mass x-ray surveys; and in promoting the routine x-raying of hospital admissions.

Dr. Meyerding's leadership and his ability to adapt the program against tuberculosis to changing methods and media have been important factors in placing Minnesota in the outstanding position it holds nationally in the sale of Christmas Seals and in carrying out the program they finance.

During the thirty-four years that he has headed the state Christmas Seal organization, he has seen the tuberculosis death rate in Minnesota drop from 69.5 per 100,000 population in 1924 to 3.6 in 1956.

* * *

Dr. Wade R. Humphrey, of Stillwater, has resigned as chairman of the Physician's Assistance Committee of the Minnesota State Medical Association because of ill health and has been replaced by **Dr. James A. Blake,** of Hopkins, who has been pinch-hitting for Dr. Humphrey as vice chairman for the past year. (See the President's message in this issue).

* * *

Dr. Gershom J. Thompson has been elected a vice president of the United States section of the International College of Surgeons.

* * *

Dr. Milton L. Kaiser, thirty-four, has been named New Ulm's outstanding young man of 1957. The selection was announced at the annual Distinguished Service Award banquet and Bosses Night program at Turner Hall. About 100 persons attended the annual Junior Chamber of Commerce project.

* * *

Dr. H. P. Linner, Minneapolis physician and surgeon, is in Temple Hospital, Philadelphia, where he underwent brain surgery to alleviate a nervous illness. Dr. Linner gave up active practice a year and a half ago because of Parkinson's disease. In recent years, his sons, Dr. John and Dr. Paul, have taken over most of his work.

* * *

Four new members of Swedish Hospital's board of trustees have been elected. They are **Dr. John S. Milton, Dr. Leonard Kendall,** C. Albert Carlson and Edward H. Norblom.

* * *

Dr. David H. Kaplan has been named chief medical

Pasteurized MIF Infant Food is Distributed to the Home Fresh and Ready to Use

INGREDIENTS

Whole cow's milk, skim milk, corn syrup solids, ferrous gluconate, activated ergosterol, vitamin A ester concentrate, thiamine hydrochloride, niacinamide, pyridoxine and ascorbic acid.

CLINICAL TESTS

MIF Infant Food in powder form has been clinically tested by the Department of Pediatrics of a well-known university*, and has been accepted as conforming to the rules of the Council on Foods and Nutrition of the American Medical Association as published in the Journal of the Association page 477, Volume 140, Number 5.
(*Name of university and results of clinical tests sent upon written request.)

APPROXIMATE ANALYSIS

Milk fat	2.60%
Milk protein	2.60%
Milk sugar (lactose)	4.20%
Dextrins, Glucose, Maltose	2.10%
Milk minerals	.62%
Calcium	850 mg. per qt.
Phosphorus	560 mg. per qt.
Iron	5.6 mg. per qt.
Water	88.0%

VITAMIN CONTENT

	Per Qt.
Vitamin A (U.S.P. units)	3000
Vitamin D (U.S.P. units)	800
Vitamin C (ascorbic acid)	100 mg.
Niacinamide	8 mg.
Riboflavin (vitamin B_2)	1.2 mg.
Thiamin (vitamin B_1)	.8 mg.
Pyridoxine (vitamin B_6)	.4 mg.

DISTRIBUTORS: Norris Creameries, Inc., Minneapolis; Sanitary Farm Dairies, Inc., St. Paul

MADE BY MAPLE ISLAND, INC., STILLWATER, MINNESOTA

officer of the Veterans Administration center at Fort Snelling. Kaplan, fifty-two, succeeds **Dr. Richard B. Hullsiek** who died February 1. Kaplan has been assistant chief medical officer at the center since 1946.

* * *

Dr. C. Walton Lillehei, University of Minnesota heart surgeon, has been chosen 1958 recipient of the Oscar B. Hunter Memorial Award of the American Therapeutic society.

The award will be conferred upon Dr. Lillehei at the society's forty-ninth annual meeting in San Francisco in June. Presentation will take place June 21, when Dr. Lillehei will address the society on his world-famous accomplishments in the repair of congenital and acquired heart defects by open heart surgery.

* * *

Dr. C. A. Saffert, president, presided at the quarterly seminar of the southern Minnesota regional chapter of the American Academy of General Practitioners at the Colony Club in New Ulm.

Speakers included **Dr. Walter P. Eter,** whose topic was "General Management of the Severely Injured Patient"; **Dr. Malcolm McCannel,** speaking on "Management of Eye Injuries"; **Dr. W. Robert Schmidt,** who chose "Management of Trauma to the Chest" as his subject; and **Dr. Lester W. Carlander,** who discussed "Management of Hand Injuries." The seminar for the southern Minnesota group was sponsored by the American College of Surgeons.

Drs. Albert and Carl J. Fritsche of the Fritsche Clinic, New Ulm, has announced the association of two more medical doctors with the clinic. They are **Drs. Peter J. Kitzberger** and **William J. Muesing,** both of New Ulm. They will have offices in the Fritsche Clinic Building, 101½ N. Minnesota. Dr. Kitzberger is a diplomate of the National Board of Medical Examiners and a member of the Minnesota Obstetrical and Gynecological Society.

Following his naval service, Dr. Muesing took four years' training as a surgical resident in the Youngstown, Ohio, Hospitals Association. He returned to New Ulm to practice with the Seifert Clinic.

* * *

Dr. John Lillie, Mayo Clinic, Rochester, Minnesota, will present a paper entitled "Thyrotomy—Technique" at the American Medical Association convention in San Francisco, June 23-27.

* * *

Dr. Gordon R. Kamman, St. Paul, addressed the Nicollet-LeSueur Counties Medical Society in St. Peter, Monday evening, March 10. His subject was "Anxiety and Depression."

* * *

Mayo Clinic staff members attending medical meetings throughout the U. S. during the past few weeks.

Dr. J. B. Brich attended a meeting of the American Fracture Assn. at St. Louis, Mo. He is a member of the board of governors of the Association.

A paper was presented by **Dr. E. V. Allen** at the postgraduate course of the American College of Physicians at Cornell University Medical School at New York.

Dr. R. K. Winkelmann presented a paper at the Second Conference on Progress and Potentials in Leprosy Investigation, held at Carville, La.

Those attending the meeting of the American Orthopsychiatric Assn. in New York City were **Dr. E. M. Litin** and **Dr. G. M. Duncan.**

* * *

"Public Health Horizons in Ramsey County" was the theme for this year's joint meeting of the area's health, welfare, planning and co-ordinating councils.

The annual meeting, held jointly by the four councils of the Greater St. Paul Community Chest and Council, Inc., was attended by over 300 professional and lay men serving the four groups.

Highlights of the meeting was a panel discussion on county health problems. The discussion was moderated by **Dr. F. M. Owens, Jr.,** and was conducted by prominent city and county health officials and members of the League of Women Voters.

* * *

Dr. and Mrs. Frederick A. Figi, Rochester have returned from a round-the-world trip of four and one-half months. During the trip Dr. Figi, emeritus member of the staff of the Mayo Clinic and former head and senior consultant of the section of plastic surgery and laryngology, gave several talks at surgical meetings and universities.

* * *

A community-wide recognition dinner honoring **Dr. Richard A. DeWall** of Minneapolis, formerly of Morris, was held recently at the West Central School of Agriculture.

Dr. DeWall's friends and former neighbors in Morris joined in the affair to pay triubute to the thirty-one-year-old research specialist whose development of a simplified mechanical heart-lung machine for use in heart surgery resulted in his selection as one of the Ten Outstanding Young Men of America for 1957 by the United States Junior Chamber of Commerce.

The dinner was sponsored by the Morris Lions Club. Invited to join the Lions were members of Kiawanis Club and the Morris Junior Chamber of Commerce, who originally nominated Dr. DeWall for the TOYM award. Wives of members of the various organizations were guests on this occasion.

* * *

Dr. David B. Robinson, a member of the Section of Psychiatry of the Mayo Clinic since October 1, 1957, will leave Rochester about June 15 to join the department of psychiatry of the State University of New York Medical School, Syracuse, N. Y.

* * *

Faculty of the Mediclinics of Minnesota, held March 2-12, 1958, in Fort Lauderdale, Florida, included: **Dr. Harold F. Buchstein,** Mr. Thomas P. Cook, **Dr. Harry B. Hall, Dr. Arthur C. Kerkhof, Dr. Francis W. Lynch, Dr. Ames W. Naslund, Dr. O. L. Norman Nelson, Dr. Owen F. Robbins, Dr. Albert V. Stoesser, Dr. Robert J. Tenner,** and **Dr. Richard L. Varco.** This year's postgraduate Medical Refresher Course was sponsored by the Florida Academy of General Practice and North Broward General Hospital.

* * *

Following are the 1958 officers of the Rice County Medical Society: President, **Dr. J. G. Beaton,** Northfield; Secretary-Treasurer, **Dr. Thorsten Smith,** Faribault; Vice President, **Dr. Wm. Furlow,** Faribault; Delegate, **Dr. Donald J. Studer,** Faribault; Alternate Delegate, **Dr. J. J. Kolara,** Faribault; and Censors, Dr. **P. G. Bauer,** Faribault; **Dr. Robert Meyer,** Kenyon, and **Dr. D. H. Petersen,** Northfield.

* * *

Dr. J. B. Beaton, Northfield internist, has been acting medical director of the Mineral Springs Tuberculosis Sanatorium at Cannon Falls since the resignation of **Dr. Ezra Bridge.** The former medical director has entered private practice in Port Huron, Michigan.

* * *

Retirement of three Mayo Clinic staff men, **Drs. Ralph K. Ghormley, Hiram E. Essex,** and **James F. Weir,** April 1, has been announced. Dr. Ghormley, an outstanding orthopedic surgeon and former head of the section of orthopedic surgery, has been at the Clinic since September, 1929. He and his wife will settle at Carmel, California, but he does not plan to continue a practice. Dr. Weir, who has been a member of the Clinic staff thirty-three years, is a former president of the staff and former chairman of four sections of medicine, with special interest in diseases of the stomach and intestines, widely recognized for his skill in physical diagnosis and particularly for his clinical work in diseases of the liver. He and Mrs. Weir will continue living in Rochester. Dr. Essex, co-chairman of the Section of Physiology and internationally known for his research work in physiology and experimental medicine, has been at the Clinic since July, 1928. He and his wife will continue living in Rochester.

* * *

Dr. Frank H. Krusen, head of the physical medicine and rehabilitation section of the Mayo Clinic, was a recent speaker at the tenth anniversary celebration of the graduate program in hospital administration sponsored by St. Louis University and the Catholic Hospital Association of the United States and Canada. He discussed "The Patient as an Individual." The entire program of the celebration was devoted to discussion of the hospital needs in an era of change in both its medical and socio-economic aspects.

* * *

Dr. and **Mrs. David B. Robinson** were featured soloists in a recent presentation of "A German Requiem" by Brahms by the Rochester Symphony Orchestra and Oratorio Society in the Mayo Civic Theater.

* * *

Dr. J. Arnold Bargen, chairman of the section of gastroenterology in the Mayo Clinic, and professor of medicine in the Mayo Foundation, has been appointed to the medical advisory board of the National Foundation for Research in Ulcerative Colitis, of Washington,

D. C. The new medical research foundation was established recently in Washington at the end of a nationwide conference on "New Frontiers in Ulcerative Colitis," sponsored by the General Medicine Study Section of the National Institute of Health and supported by a research grant from the new foundation and from the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

* * *

Drs. Truman and Homar H. Hedemark, Ortonville, announced the association of **Dr. George V. Martin** with them in the practice of medicine and surgery at the Hedemark Clinic.

* * *

Dr. O. Theron Clagett, head of a section of surgery in the Mayo Clinic and professor of surgery in the Mayo Foundation, was elected to honorary membership in the Irish College of Surgeons at the Charter Day meeting held in Dublin, February 15. At the meeting he also delivered the Abraham Colles Lecture, named for the celebrated Irish surgeon, who was president of the College of Surgeons before he died in 1843.

* * *

Dr. Jan H. Tillisch of the Mayo Clinic staff was one of nineteen American educators and businessmen who served as the Air University's Board of Visitors in conducting the fourteenth examination of the Air Force's professional education system at Maxwell Air Force Base, Montgomery, Alabama, recently.

DOCTOR'S HOME BECOMES MELTING POT

A Saint Paul physician's home is turning out to be a strange melting pot of Japanese and American cultures. American culture is rubbing off on Hisachika Hirose, seventeen, a Japanese exchange student at Sibley high school, while customs of his native land are making an equally strong imprint on the family of **Dr. and Mrs. M. B. Sorem,** 606 Sibley Hwy., Mendota Heights. Hisachika, a bespectacled lad with a ready smile and ingratiating manners, is making his home with the Sorems while studying as a senior at Sibley high. He's taking to the American tempo and ways of doing things like the proverbial duck to water. A bright student Hisachika is earning straight A's at school despite the linguistic barrier and he's making an equally smooth adjustment to other phases of American living.

Hisachika, whose only apparent difficulty here lies in finding the rare thing that he doesn't like, is particularly captivated with the informality of American schools. He's even critical of the way things are done in Japan when he compares the two educational systems. "Teachers are very friendly in the classrooms here," declared Hisachika, "and they discuss a wide range of subjects outside the course itself. However, in Japan the schools are too formal, with everything too rigid. Relations between teachers and student are never friendly." Another difference appealing to the Japanese youth, whose home is a two hour train ride east of Osaka, is the relatively easier American school work

The purity, the wholesomeness, the quality of Coca-Cola as refreshment has helped make Coke the best-loved sparkling drink in all the world.
DRINK
Coca-Cola
REG. U.S. PAT. OFF.
SIGN OF GOOD TASTE

Brown & Day, Inc.

You are Cordially
INVITED
to attend our Booths at the
UPPER MIDWEST
HOSPITAL CONFERENCE
May 14, 15, 16
and the
MINNESOTA STATE
MEDICAL ASSOCIATION
May 22, 23, 24

"Everything for the Physician"

for fast service call
CA 2-1843

BROWN & DAY INC. SAINT PAUL
SERVICE QUALITY
62-64 EAST 5TH ST
St. Paul 1, Minn.

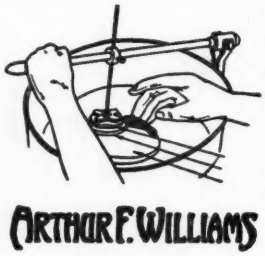
ORTHOPEDIC APPLIANCES

Skill and care combine with quality materials in all Buchstein-Medcalf orthopedic appliances. Our workmanship and scientific design conform to the most exacting professional specifications. Accepted and appreciated by physicians and their patients for more than 45 years.

ARTIFICIAL LIMBS, TRUSSES
SUPPORTERS, ELASTIC HOSIERY
Prompt, painstaking service

Buchstein-Medcalf Co.
223 So. 6th St. Minneapolis 2, Minn.

UNUSUAL LENS GRINDING



CATARACT,
MYO-THIN
and other difficult and complicated lenses are ground to extreme thinness and accuracy by our expert workmen.

ARTHUR F. WILLIAMS
SAINT PAUL
MINNESOTA

load. Hisachika disclosed there is much more emphasis on science and languages in Japan than in America.

For example, Hisachika started studying English in the seventh grade in Japan and had five years of the subject before coming to the U.S. as an exchange student last August. Students wear standard uniforms in Japan, as compared with the great variety of dress used here and little attention is paid to extra-curricular activities. School spirit is practically non-existent in the Japanese high school as compared with its American counterpart, according to Hisachika. "I was surprised when I first came here to see all girl cheerleaders," said Hisachika. "In Japan, girls are too quiet to be cheerleaders. Anyway, there are no cheerleaders in Japan." Elvis Presley and rock and roll are popular with Japanese teen-agers but ballroom-style dancing is practically unheard of except in the larger cities, Hisachika revealed. Hisachika is fitting like a glove into the pattern of American living—both at school and in the Sorem home. The Sorems regard him as one of the family and Hisachika does, too. He constantly refers to Mrs. Sorem as his American "mother."

Although he is scheduled to become a Shinto priest when his grandfather dies, Hisachika has a keen interest in Christianity and attends Hamline Methodist church regularly on Sundays with the Sorems. Hisachika shares a bedroom, chores and other facets of family life with the Sorems's son, Anthony, seventeen, a junior at Sibley high and the two youngsters "are devoted to each other," according to Mrs. Sorem. But it's not entirely a question of Hisachika adjusting to American ways, and the Japanese lad has introduced more than a few innovations in his new American home.

"He's got us eating with chopsticks," smiled Mrs. Sorem, by way of emphasizing that point . . . "Hisachika cooked sukiyaki for us recently and we all thought it was wonderful." Sukiyaki is comparable to American beef stew—with strips of beef and vegetables cooked together. Hisachika is one of a group of forty-nine Japanese students who flew to the U.S. last August to attend American high schools in a program sponsored by American Field Service. Five of the forty-nine Japanese students are attending school in Minnesota. Mrs. Sorem, a member of the American Field Service committee in the St. Paul area, said the foreign students do not come here to be honorary guests in an American home. "These students come here," she continued, "to learn about America and the community in which they live. When they return to Japan next July they will be ambassadors of good will."

She said there is a great need for families in this area to take one of these foreign exchange students into their homes "as an investment in the future." The exchange program provides for American high school students going to foreign countries during the summer months to live with families of those countries. And Mrs. Sorem is convinced that the program is an important instrument in the promotion of world peace. (This news feature appeared in the *St. Paul Dispatch*, Friday, Feb. 1, 1958).

Book Reviews

Books listed here become the property of the Ramsey, Hennepin and St. Louis County Medical Libraries when reviewed. Members, however, are urged to write reviews of any or every recent book which may be of interest to physicians.

MODERN PERINATAL CARE. By Leslie V. Dill, M.D., F.A.C.S., Diplomate of the American Board of Obstetrics and Gynecology. 309 pages. Illus. Price $6.50. New York: Appleton-Century-Crofts, Inc., 1957.

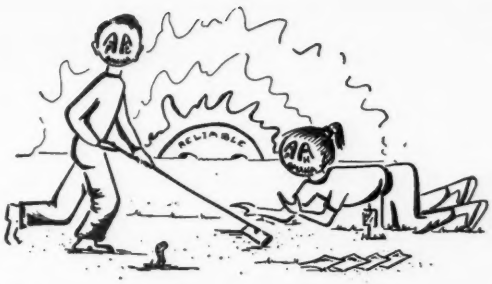
According to the preface, this book has as its aim the crystalization of present-day thought on antepartum and postpartum care. The word "modern" in the title in this case denotes "current." In addition, this book was designed for the utilitarian purpose of giving aid to those practitioners for whom consultation is not readily available.

The book is divided into twenty-one chapters which, among others, include: Manifestations of Pregnancy, Hygiene and Nutrition of Pregnancy, Abortion, Pelvic Mensuration, Psychology of Pregnancy as well as chapters on the common medical complications of pregnancy, the fourth stage of labor, fetal and neonatal mortality, erythroblastosis, infant feeding and obstetric records. In addition, there is a chapter on the practice of obstetrics and the law written by Professor Thomas O'Connell of the Law School of Georgetown University which seeks to define the areas in which malpractice and other legal complications are most likely to arise in obstetric practices. There is also a chapter on the ethics of the Catholic Church pertaining to obstetrics, which was reviewed and edited by three authorities from the Catholic Church. This chapter is especially welcome since there seems to be considerable confusion in the minds of many practitioners, both inside and outside the Catholic Church, regarding the ethics of the Church toward problems involving the care of the pregnant woman.

As is to be expected from a book which seeks to cover so much territory in so few pages, the text tends to be more factual than discursive. The graphs are beautiful in their simplicity. However, the documentation on which some of the charts are based is not always clear, and apparently the author has taken average values from certain references in literature plus his own experiences. This, of course, may not always be valid. There are some chapters which would perhaps evoke some disagreement; notably the chapter on the anemias which does not discuss the knowledge made available by the use of parenteral iron, and the chapter on x-ray pelvimetry which may have to be revised in the light of increasing known hazards of irradiation of the pregnant uterus.

The book is well written, concise, and shows the results of careful editing. I think it succeeds in the task set for it, and I think it can be recommended without reservation for the intern, the resident, and the busy general practitioner.

ERICK Y. HAKANSON, M.D.



Protection against loss of income from accident & sickness as well as hospital expense benefits for you and all your eligible dependents.

ALL PREMIUMS COME FROM PHYSICIANS SURGEONS DENTISTS ALL BENEFITS GO TO

PHYSICIANS CASUALTY & HEALTH ASSOCIATIONS

OMAHA 31, NEBRASKA

Since 1902

Malpractice Prophylaxis

IT'S NOT AN ACCIDENT
our claims and suits
go down while elsewhere they go up

Specialized Service makes our doctor safer

THE MEDICAL PROTECTIVE COMPANY
FORT WAYNE, INDIANA

Professional Protection Exclusively since 1899

MINNEAPOLIS Office:
Charles A. Greenwood, Rep.
P.O. Box 8415
St. Louis Park Station
Telephone Federal 9-1292

Classified Advertising

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *2642 University Avenue, Saint Paul 14, Minnesota.*

WANTED GENERAL PRACTITIONER—Twin Cities suburban area. New clinic building. Immediate opening. Address E-613, care MINNESOTA MEDICINE.

GENERAL PRACTITIONERS—Two capable generalists needed for complete practice—expanding group serving three communities. New clinic facilities, new accredited hospitals. Specialist consultant available in group and expert radiologists and pathologists. Full hospital privileges immediately. Progressive area, finest schools and churches. Good recreational area, hunting and fishing. Salary open. Partnership possible within three years. Contact Mr. James Streitz, Manager, Mesaba Clinic, Hibbing, Minnesota.

PROMPT FULL PARTNERSHIP in general practice in Minneapolis suburb of Bloomington. Present population near 40,000, still growing. Harley J. Racer, M.D., The Village Center, 78th & Penn, Minneapolis 20, Minnesota. Telephone UNion 6-8731.

A VACANCY for one medical doctor exists at the Good Thunder Medical Center. Some of the necessary equipment and fixtures can be available. Call or write Good Thunder Area Developments, Inc., S. E. Kienitz, President or H. E. Glaeser, Telephone 2711.

GENERAL SURGEON—To join general practice group of young physicians; outstanding clinical facilities; new building Saint Paul, Minnesota; salary initially; early partnership desired. Address E-626, care MINNESOTA MEDICINE.

GENERAL PRACTICE-PEDIATRICS—Young G.P.—interest Pediatrics—join two young G.P.'s interests Obstetrics, Gynecology, Medicine; new modern office building; salary to start; early partnership desired; Saint Paul, Minnesota. Address E-627, care MINNESOTA MEDICINE.

CHALLENGING OPPORTUNITIES in Anoka State Hospital.—Active treatment program including psychiatric, medical, and surgical care with growing research programs. Apply now for psychiatrist and physician openings under revised salary plan. Write Dr. Donald B. Peterson, Superintendent, Anoka State Hospital, Box 11, Anoka, Minnesota, or Minnesota Civil Service Department, 122 State Office Building, Saint Paul, Minnesota.

WANTED—Physician with experience in general practice or training in internal medicine to become associated with four-man established clinic. Address E-617, care MINNESOTA MEDICINE.

WANTED—General practitioner to join six-man group caring for mining company's employes and families. Includes general practice, obstetrics, surgery and industrial work. Salary $10,000 per year to start. All equipment and car furnished. Living conditions and schools excellent. Location—Black Hills. Immediate opening. Call or write: N. W. Stewart, M.D., Chief Surgeon, Homestake Mining Company, Lead, South Dakota.

PHYSICIAN WANTED—In suburban Saint Paul. New modern office available. Monthly rental $110.00, includes air conditioning and heat. In reply, please state age, background and religion. Write: James A. Haiden, D.D.S., 400 East Little Canada Road, Saint Paul 17, Minnesota.

FOR RENT—Medical office, occupied by physician past seventeen years, at 1583 North Hamline, Saint Paul. Write or telephone Robert Blomberg, 1481 West Hoyt, Saint Paul 13, Minnesota, MIdway 6-2034.

FOR SALE—Keleket x-ray 100 M.A., in best of condition. H. K. Helseth, M.D., Box 157, Fergus Falls, Minnesota.

FOR SALE—Office equipment purchased in 1956, used 15 months, at big discount. Includes Picker Century II x-ray with rotating anode, motor-driven table, fluoroscope automatic control, and accessories. Will sell for half list price. Also AO Spencer binocular microscope, Lumetron colorimeter, and other items. Address E-628, care MINNESOTA MEDICINE.

FOR SALE—Six-room completely equipped clinic, general practice, open hospital, county seat town. Home and modern winterized cottage—optional. Moderate down payment. Personal reason for selling. Address E-618, care MINNESOTA MEDICINE.

FOR SALE—Good practice and adequate equipment in town with excellent hospital. Will help to get started. Low down payment and easy terms. Would like to retire, but will consider assistant with military obligations completed. Address E-623, care MINNESOTA MEDICINE.

FOR SALE—Sisk G-U table with Bucky and Continental x-ray unit—100 milliamperes. Slightly used. Address E-624, care MINNESOTA MEDICINE.

FOR SALE—Collected Papers of the Mayo Clinic. 50 volumes 1905-1956. $300.00. Address E-625, care MINNESOTA MEDICINE.

FOR SALE—Violins and bows—rare and select. Telephone (Saint Paul) MElrose 3-1592.

FOR SALE—Completely equipped office, southern Minnesota city, 9,000 population. $20,000 gross annually. Address E-621, care MINNESOTA MEDICINE.

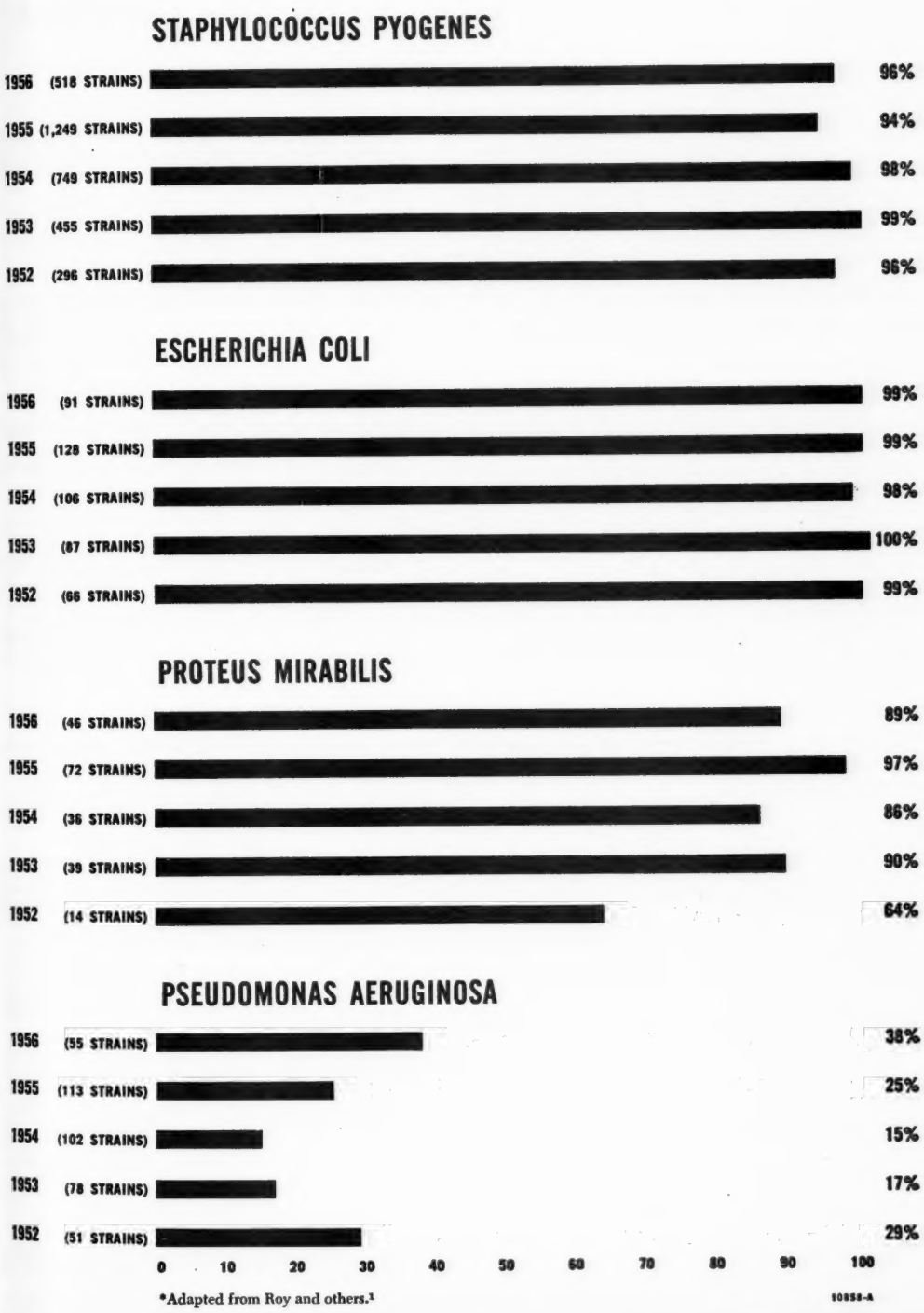
FOR SALE OR RENT—Small office building, 2 years old, suitable for physician, in flourishing southern Minnesota town of 7,500. New hospital being erected. Good opening for physician or surgeon. Address E-622, care MINNESOTA MEDICINE.

FOR SALE—Office equipment and instruments. Waiting room, office, surgery, physiotherapy and x-ray equipment. Reasonable price. Address E-620, care MINNESOTA MEDICINE.

PLACEMENT SERVICE

The Minnesota State Medical Association maintains a Medical Placement Service for the benefit of physicians who are looking for locations and positions; also for communities, medical groups and physicians who are looking for licensed medical assistance. For information, write to the Minnesota State Medical Association, 496 Lowry Medical Arts Bldg., Saint Paul 2, Minnesota.

IN VITRO SENSITIVITY OF FOUR COMMON PATHOGENS TO CHLOROMYCETIN FROM 1952 TO 1956*


STAPHYLOCOCCUS PYOGENES
1956 (518 STRAINS) 96%
1955 (1,249 STRAINS) 94%
1954 (749 STRAINS) 98%
1953 (455 STRAINS) 99%
1952 (296 STRAINS) 96%
ESCHERICHIA COLI
1956 (91 STRAINS) 99%
1955 (128 STRAINS) 99%
1954 (106 STRAINS) 98%
1953 (87 STRAINS) 100%
1952 (66 STRAINS) 99%
PROTEUS MIRABILIS
1956 (46 STRAINS) 89%
1955 (72 STRAINS) 97%
1954 (36 STRAINS) 86%
1953 (39 STRAINS) 90%
1952 (14 STRAINS) 64%
PSEUDOMONAS AERUGINOSA
1956 (55 STRAINS) 38%
1955 (113 STRAINS) 25%
1954 (102 STRAINS) 15%
1953 (78 STRAINS) 17%
1952 (51 STRAINS) 29%
0 10 20 30 40 50 60 70 80 90 100

*Adapted from Roy and others.[1]

10858-A